



WO 142 R839p 1923

46310890R

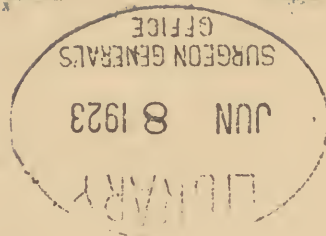


NLM 05236749 1

NATIONAL LIBRARY OF MEDICINE

B15-4-8

SURGEON GENERAL'S OFFICE	
LIBRARY.	
Section	<i>Surg, Path</i>
No. 113, W. D. S. G. O.	No. <i>245157</i>
3-513	











ROST'S  
PATHOLOGICAL PHYSIOLOGY  
OF SURGICAL DISEASES

---

REIMANN



THE  
PATHOLOGICAL PHYSIOLOGY  
OF  
SURGICAL DISEASES

*A Basis for Diagnosis and Treatment of Surgical Affections*

BY  
PROFESSOR DR. FRANZ ROST  
*University of Heidelberg*

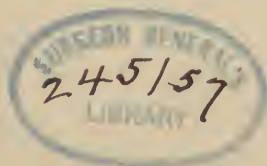
AUTHORIZED TRANSLATION

BY  
STANLEY P. REIMANN M. D.  
*Chief of Pathological Department of the Lankenau Hospital and Assistant Professor  
of Experimental Pathology, University of Pennsylvania, Philadelphia, Pennsylvania*

WITH A FOREWORD

BY  
JOHN B. DEEVER, M. D., LL. D., Sc. D., F. A. C. S.

PHILADELPHIA  
P. BLAKISTON'S SON & CO.  
1012 WALNUT STREET



W0  
142  
R839 P  
1923

COPYRIGHT, 1923, BY P. BLAKISTON'S SON & CO.

PRINTED IN U. S. A.  
BY THE MAPLE PRESS YORK PA

© C1 A696912 R  
MAR 26 '23

no 2

## AUTHOR'S PREFACE

This text book has been evolved from teaching. When a teacher comes into close relation with his students, he quickly sees the need for an exposition of surgical questions from a somewhat generalized pathological anatomical viewpoint, as is done, more or less routinely, in internal medicine. It is not sufficient for the student to know that a patient may live without an organ, that he may tolerate, for example, a total resection of the stomach; he also wants to know the manner in which nature balances and compensates those defects, often extensive, that are caused by operation. In the ordinary text books, there is little information on this subject, and the student has no time for special studies.

But it is not merely the stimulation to thought which makes desirable the discussion of such pathological physiological questions. Surgical teaching, more than any other, should be a "viewpoint teaching." The student receives an endless number of single isolated impressions, which he absorbs, in general, as a feat of memory. Experience, memory pictures, must necessarily constitute the greater part of the teaching of external diseases, but in the time usually allotted to the study of the wide field of surgery, only a superficial amount of knowledge can be acquired. Doubtless this is the principal way to teach surgery, and it must remain so, but the thing most often lacking is a comprehension of the peculiarity of surgical thought.

In surgery, as in no other branch of medicine, the pathological changes are actually seen daily. The surgeon disturbs the various mechanisms of the body by his operative procedures, and in cases operated too late, sees the final picture, and thus evolves a personal conception of the causes and effects of disease. Herein lies the peculiar specificity of surgical thought based on observations of life processes in organisms changed by disease, and their reaction to the special methods used in surgery. It is most important for the student to be able to follow the mental processes of the surgeon; in other words, not only should he be trained "mechanically" in the art of surgery, but "intellectually" as well. Only then will he be able to estimate correctly which diseases are amenable to surgical treatment, when interference is most useful, and how best to proceed even when he sees a case which has not been presented to him in his student days. The purpose of this book is to provide a link between the student and physician, in the interpretation of diseases of the human body.

But it is not only the student who finds it difficult to obtain information on any pathological physiological question, but also the young assistant; indeed even the independent surgeon finds it difficult if there is no complete library in his locality. The literature containing this material is scattered in the periodicals of the most diverse specialties of medicine. A valuable treasure house of pathological physiological work is contained in surgical literature itself, because much special investigation has been done from the surgical standpoint.

The importance of such questions is continually increasing. Surgical technique, which is essentially well standardized and thoroughly treated in the ordinary text books, is not especially difficult to master with a fairly skilled hand and a keenly observant eye. Technique alone does not make a good surgeon; to it must be added the faculty of judging the strength of the patient in reference to the severity of the proposed operation, the courage and knowledge to deal with unforeseen circumstances, the ability to determine swiftly the most suitable treatment, and many other things. These all require an extensive knowledge and understanding of physiology, indeed it is only by a broadening of physiological conceptions, that progress in surgery may be expected.

In this book purely technical matters, that is, animal experiments covering operative methods, have been discussed only when pathological physiological questions were involved. Furthermore, I have omitted or merely mentioned subjects which are treated completely in the usual text books, for example, transplantations, regenerations, rachitis, etc. It was not always easy to draw a boundary line.

I have worked on this book for seven years, but feel at this time of publication, the painful sensation of having perhaps overlooked many important works. I shall be grateful for advice on these points.

I must express my thanks to all those gentlemen in whose institutions and clinics I obtained, as assistant, the knowledge which enabled me to write this book. These gentlemen are Geh. Rat. Prof. Dr. Knauf and Prof. R. O. Neumann (Hygienisch-bacteriologisches Institut, Heidelberg), Prof. Dr. Weintraud (Innere Abteilung des Stadt. Krankenhauses, Wiesbaden); Geh. Rat. Prof. Dr. Furbinger (Anatomisches Institut Heidelberg); Geh. Rat. Prof. Dr. Schmorl (Pathologisch-anatomisches Institut, Dresden-Friedrichstadt); Geh. Rat. Prof. Dr. Enderlen (Chirurgische Universitätsklinik, Heidelberg).

I also thank the publishers for their great kindness during the preparation of the work.

FRANZ ROST.

HEIDELBERG.



## TRANSLATOR'S PREFACE

This book has appealed to us for a number of reasons, chief of which is the fact that questions such as are discussed in it have confronted us in our hospital work, many times. It has been the desire of the staff of the pathological department of the Lankenau Hospital to have the department regarded, in addition to its other uses, as a sort of clearing house for information . . . a place in which the many questions arising in daily clinical work, not only on the surgical service, but on the other services of the hospital as well, could be discussed and answers found, if possible. In other words, we have undertaken the rather difficult task of seeking for explanations of phenomena met with in the wards, when such explanations were not forthcoming from our previous experience or knowledge. To us it seemed that this book filled considerable need, not only in its discussion of many of the subjects, but also in its direct reference to a rather extended bibliography, a bibliography with which we were not as familiar as with the writings in our own language.

This is not a literal translation, but it is hoped that the spirit of the sentences is preserved, especially in reference to the general underlying idea of the way the author has expressed himself. I mean particularly the style or philosophical system of his expression. It is, of course, understood that by "explanation" in science is meant the gathering together of a group of facts under the application of more general laws. It will be found that the author is very fond of using such expressions as indicate the purposefulness of many of the phenomena which he discusses. He does not insist on a mechanistic explanation of his facts, but recognizes the incompleteness and short-comings of such endeavors. This is the spirit which I have attempted to preserve in the English translation. Much stress has been laid for many years upon the idea that when an explanation for a phenomenon is not immediately forthcoming in mechanistic terms, that is, in terms of matter or motion, it is highly dangerous, disadvantageous and obstructive to progress to assume that there is a "vital" process concerned. It is said that this idea hinders further investigative work. It seems forced to me, however, to regard this assumption as such a bugaboo, especially when applied to a clinico-investigative field in which we may happen to deal with arranged,

classified and more or less generalized knowledge, but must perforce use this knowledge in connection with patients, each one an individual, and a problem in himself. At least, that is our idea of the best way of treating a sick human being. It is interesting to observe the emphasis laid by the author upon the power of the nervous system. It is also interesting to consider the emphasis which he so often places upon individual predispositions. In this connection, it is most interesting to read Karl Pearson's well known book, "The Grammar of Science," as well as J. Arthur Thompson's text, "The System of Animate Nature."

It occurred to me while translating this book, that some additions might be added, regarding the subjects with which we, in our hospital work, have had more experience than certain others. These additions by the translator are bracketed. It may well be objected that the literature quoted is German almost exclusively, with very few references in other languages. An attempt was made in one chapter, that on the stomach, to review an extensive bibliography of publications in the English language, but it was found after the task had been finished, one which took many months, that it was scarcely worth the trouble. The references were easily found, and when read, actually it was discovered that the same viewpoints were expressed as in the text; in other words, it was thought that the object of the book in this particular field, namely, to present various viewpoints on any particular problem, was complete enough to allow anyone interested in those points to easily work them up in more detail by himself. Many of the references are what we may consider old. A professor of English, whom I knew very well, often said in reference to the use of words, that it is better to use the oldest of the new and the newest of the old. This, it appears to me, is important; therefore, in this book, we have been conservative regarding the discussion of new work. Just to mention an example, the preparation of insulin from the islands of Langerhans of the pancreas might very well have been mentioned, but on the other hand, if all, or even a large part, of the very new things had been put in, the book could very well have attained enormous proportions, not to speak of the great amount of time necessary for the gathering together of the data, after which still newer work would be reported, and so on, *ad infinitum*. In the special case of insulin, it was thought better to wait for fuller information and more definite conclusions, and this was the rule with many other cases.

I wish to acknowledge my indebtedness to members of the staff of the hospital and to certain of my colleagues at the University of Pennsylvania for assistance and advice in reference to many of the points. In the

hospital, I must mention in particular, Dr. Carl E. Becker and Miss Lida Snellbaker for their cheerful and most valuable help throughout the entire preparation of the translation. To Miss Maude T. Shutt, I must also express gratitude for her tireless help in the stenographic work. Finally, the publishers also deserve my thanks for their many courtesies.



## FOREWORD

BY JOHN B. DEAVER, M. D., LL. D., SC. D., F. A. C. S.

It is a self-evident fact that good surgery demands of the surgeon not only nicety of judgment and faultless technique, but also a working knowledge of physiology, pathology, and bacteriology for purposes of diagnosis as well as for the important matter of postoperative results. This principle forms the basis of the comprehensive work of Rost now available to surgical English readers.

This systematic treatise makes no attempt to indicate practical technique of surgery, but is devoted to a discussion of the principles underlying diagnosis as well as operative methods.

As a guide to surgical diagnosis it aims to outline general facts which can be applied to specific cases, so that although a practitioner may be unacquainted with a given condition, he will find that the general knowledge of the essential features of that particular group of diseases herein presented, will enable him to treat his patients more intelligently and consequently more satisfactorily than otherwise.

As a guide to the proper surgical measures to be applied in a given case, it aims to present the physiologic effects of surgery, inasmuch as it discusses nature's method of compensation for and defense against the effects of man's interference. These effects are amply illustrated by animal experimentation by the author himself, as well as by examples taken from the literature. Observations on the living human subject at the operating table have advanced so far that the surgeon is often enough now in a position to note the results of surgical treatment at a period more or less remote to a previous intervention. The deductions derived from such observations are without doubt the most valuable contributions to practical medicine and surgery of our times.

The citations are voluminous and of themselves make available to the research worker in collected form the results of experimental and practical work in normal and pathologic physiology, that are scattered in journals, textbooks, and treatises, which few have either the time or the opportunity to collect and digest.

The scope of the book includes every region of the body amenable to surgery, and will no doubt prove useful to the student, the general practitioner, the general surgeon as well as to the specialist in surgery.

Only a thorough-going thoughtful scientist, imbued with the sense that science knows no geographical or national limitations could so enthusiastically have undertaken the translation of the work at this time and carried it to such successful conclusion. He has rendered the thoughts of the author in simple illuminating language in this English edition of Rost which is herewith presented to the public.

JOHN B. DEAVER.

# CONTENTS

## CHAPTER I

	PAGE
ORAL CAVITY. SALIVARY GLANDS. TONGUE AND ESOPHAGUS. . . . .	I
Literature . . . . .	31

## CHAPTER II

STOMACH . . . . .	36
Literature . . . . .	81

## CHAPTER III

PANCREAS. . . . .	95
Literature . . . . .	106

## CHAPTER IV

LIVER AND GALL BLADDER. . . . .	110
Literature . . . . .	141

## CHAPTER V

SPLEEN . . . . .	148
Literature . . . . .	158

## CHAPTER VI

PERITONEUM. . . . .	161
Literature . . . . .	186

## CHAPTER VII

INTESTINES . . . . .	190
Literature . . . . .	269

## CHAPTER VIII

KIDNEYS, BLADDER, MALE GENITALIA. HYPOPHYSIS. . . . .	279
Literature . . . . .	330

## CHAPTER IX

	PAGE
THYROID GLAND . . . . .	338
Literature . . . . .	366

## CHAPTER X

CHEST CAVITY . . . . .	372
Literature . . . . .	398

## CHAPTER XI

BRAIN AND SPINAL CORD . . . . .	403
Literature . . . . .	423

## CHAPTER XII

EXTREMITIES. . . . .	427
Literature . . . . .	483
INDEX OF AUTHORS . . . . .	493
SUBJECT INDEX . . . . .	515



# THE PATHOLOGICAL PHYSIOLOGY OF SURGICAL DISEASES

## CHAPTER I

### DIGESTIVE ORGANS

#### ORAL CAVITY, SALIVARY GLANDS, TONGUE AND ESOPHAGUS

Digestion begins in the **mouth**. With the assistance of teeth, tongue and cheeks, the food is comminuted, molded and thoroughly mixed with the first digestive secretion—**saliva** (1). This fluid is a product of the parotid, submaxillary and sublingual glands, and these organs are of particular interest from the standpoint of the study of glandular secretion for, on account of their accessibility and the ease with which their products can be collected, they have early provided classical material for the study of secretion in general. Foremost among the investigators in this subject are Ludwig (2) and Heidenhain (3) upon whose fundamental work numerous followers have built. The first observations of the detailed processes which occur in cells during activity were investigated microscopically in the salivary glands.

The *innervation* of these structures is from two sources; sympathetic fibres from the carotid plexus and autonomic fibres from the glossopharyngeal nerve. According to Kohnstamm (4), the submaxillary gland is controlled by a special center which lies between the nucleus of the facial nerve and the motor trigeminal (nucleus salivatorius). Fibres from the nucleus travel at first with the pars intermedia of the facialis and then as the chorda tympani of the lingual nerve.

The fibres to the parotid arise in the petrosal ganglia of the glossopharyngeal as the tympanic, and continue as the superficial petrosal minor nerve to the otic ganglion of the trifacial. The parotid is supplied from this ganglion through the auriculotemporal nerve. Proof that all the secretory fibres to the parotid are supplied through this particular nerve, was first given by Claude Bernard. From the practical point of view, Leriche (5) and later Troncy (6) deduced that the secretion in salivary fistulæ could be abolished by section of the nerve, which fortunately is not difficult to find. The results were good. During the

war, this operation was occasionally performed to control unbearable salivation (7).

Glossopharyngeal saliva is serous and contains very few salivary corpuscles. It has the very interesting property of being about  $1\frac{1}{2}$  degrees warmer than the blood in the carotid artery, a proof that the formation of saliva is not merely a filtration but is coincident with considerable oxidation within the gland. These investigations were made chiefly on the submaxillary gland of dogs but the same principles apply to the parotid gland. Stimulation of the tympanic, that is, the superficial minor petrosal nerve, gives results similar to those obtained in the submaxillary glands by stimulation of the chorda. The processes in the three salivary glands may therefore be discussed jointly.

Stimulation of the chorda produces marked dilatation of the vessels within the submaxillary gland and the saliva secreted is serous. Stimulation of the sympathetic fibres which accompany the blood vessels gives rise to a scanty amount of stringy saliva with considerable mucus. Stimulation of the sympathetic in the neck causes a marked constriction of the blood vessels.

Under normal conditions, secretion is reflex, and occurs from the cortex, as shown in the flow of saliva initiated by seeing or smelling palatable food. Stimulation at the periphery, especially in the mouth and throat also brings about secretion. The salivation in stomatitis and after injuries to the oral mucosa is well known. But impulses originating in other parts of the body may also cause salivation. Thus, according to Gaultier (8), there is often marked salivary secretion in a very early stage of esophageal carcinoma, and similarly, according to the same author, the often troublesome salivation during esophagoscopy is explained by the same reflex relation between the esophagus and the salivary glands.

These nerve impulses regulate not only the *quantity* but also the *quality* of the saliva to an extraordinarily delicate degree. Pawlow (9) found the response to dry food greater than to moist food, and strongly stimulating substances such as acids, excited considerable salivary secretion. But it was not even necessary to bring these substances into actual contact with the oral mucosa. Secretion followed when an animal was offered food with which he was familiar by sight. Brunacci (10) has recorded the qualitative changes in his own saliva which followed the application of various stimuli. That which was secreted under mechanical stimulation differed the widest from that produced by sour substances, and between these extremes, all possible varieties were poured out. According to Popielski (11), the amount of saliva produced on stimulation by acids, is in direct proportion to the number of hydrogen ions present, irrespective of the kind of acid. It might be mentioned that ether is one

of the substances which produces a marked flow of saliva through stimulation of the oral mucosa, and consequently there is considerable salivation in the early stages of anesthesia.

This interesting adjustment of the quality and quantity secreted after different peripheral stimuli, has been further investigated by Jappeli (12), who found that differences in the physicochemical composition depend on stimulation of different areas in the central nervous system. Furthermore, he found that a flow of saliva could not only be stimulated from the brain and cerebellum, but also inhibited. It is quite possible, though not known, that the diminution observed in fever may be attributed to irritation of these inhibitory centers (13), though the diminution in deep anesthesia is probably not caused by such depression. In addition to being under nervous control, the quantity and concentration is also dependent on the water content of the blood (14). Thus there is dryness of the mouth after perspiration, and this in its turn leads to the sensation of thirst.

Investigations of the chemical composition of normal saliva have been extensive and accurate, and will be dealt with later (15). In studying salivary secretion, particularly by means of chemical analyses, it is very important to remember that there are constant normal changes during the day in both the quantity and composition, especially of the enzymes (16). [A distinction should also be made between mixed saliva and the saliva from the individual glands.]

What *functional significance* has this secretion? Beginning with the observation that lesions in the mouth usually heal promptly although they are by no means aseptic, and that in dogs primary healing of almost any kind of a wound takes place when the animal can lick the site, and finally that many plant seeds will not germinate if saliva has been added to the earth (17), the conclusion is almost forced that the saliva must have powerful *antiseptic action*. But in spite of considerable experimental work, first by Sanarelli, and recently by Clairmont (18), who also reviews the investigations of former authors, the question is not definitely settled. According to the latter, the saliva has no actual bactericidal power. Nevertheless, a number of bacteria, among them the common pyogenic staphylococci and streptococci find saliva an unfavorable medium for growth. The latter grow in long chains and this seems a sign of injury. On the other hand, certain bacteria, such as pneumococci grow, well so that Grawitz and Steffen (19) recommend its addition to culture media. The saliva with the strongest disinfecting power is secreted by the parotid gland, according to the experiments of Clairmont (18). The chemical substance usually held responsible for this action is potassium sulphocyanid. It is said to arise from nitrogenous metabolism, but the details cannot be elaborated here (20). Suffice it to say that a compound is then

supposed to be formed which has stronger bactericidal power than the simple substance itself. The objection has, of course, been raised that potassium sulphocyanid is inactive in the strength in which it is present in the saliva, but this does not seem to have been satisfactorily proved. The influence which substances may have on bacteria within the animal body can never be safely judged by their influence in the test tube, for substances entirely inactive in the latter may be strongly bactericidal in the animal body, or *vice versa*.

The sulphocyanid content in smokers is greater than in non-smokers (15) and as Clairmont has shown, the addition of food to saliva completely neutralizes its bactericidal effect. Particles of food are also good culture media. Mechanical cleansing of the mouth after every meal is therefore advisable.

In addition to its effects on bacteria, saliva shows a *destructive action on certain toxins*. Wehrmann (21) demonstrated, for instance, a loss of the destructive action of the venom of snakes, and Carriere (22) found the same with tetanus toxin.

These, and other similar experiments have thus given a certain amount of explanatory evidence for the numerous clinical observations that wounds of the mouth heal unexpectedly well, but Gottlieb and Siches (23) showed that injuries to the mouths of dogs heal just as well if the salivary glands have been extirpated, or their ducts ligated. From this it seems to follow, that the quick healing of wounds in this part of the body does not depend on the presence of saliva and that its value in wound healing must not be overestimated. For the present, the subject must rest here.

The *significance of saliva in digestion* is given ratings which differ greatly. In general, the more accurate investigations of later years have shown that, in reality, it plays quite an important part, and that it was unjustly underrated for a long time. In the first place, by reason of its water content, it acts as a solvent for various food stuffs (15); with its help the bolus is formed, made slippery, and fit to be swallowed. [There are those who believe that this is its most important function.] It helps the sense of smell. It is easily reabsorbed in the stomach and Hammarsten believes that it carries dissolved substances with it. Its alkaline reaction can diminish the acidity of foods, [fermentative products or regurgitated stomach contents, and thus protect the teeth], and finally it contains an amylolytic enzyme which splits starch into sugar, and this may be considered its most important function. [However, as Luciani remarks (24), the saliva of carnivora as that of infants is destitute of ptyalin as might be expected from teleological considerations, and this is the best proof that the principal function of saliva is mechanical, *i.e.*, formation



of the bolus. Attempts to show that the saliva of dogs, for example, developed amylolytic power when carbohydrate diet was given have been refuted.] The ptyalin may, however, be very active, as shown by Salkowski and others (25) and according to the well known findings of Grutzner, its action may continue in the stomach, since the food admixed with saliva is deposited in that organ in such a manner that the bolus last swallowed forms the central part of the mass. Hydrochloric acid, therefore, which inhibits its action, does not reach the center for some time and thus carbohydrate digestion continues in this portion of the stomach contents, contrary to the former view that ptyalin was destroyed as soon as it reached the stomach (Claude Bernard).

Still another property has been assigned to saliva, namely, that of stimulating the production of hydrochloric acid in the stomach. Stricker, and later Biernacki (26) found that the quantity of this acid secreted after feeding through a stomach tube was less than that produced following naturally chewed and swallowed food. In such experimental methods, however, psychic factors cannot be excluded and we know from the work of Pawlow, and others, that these factors have considerable influence on gastric secretion (see later). [The alleged presence of a gastric hormone has also been refuted.]

The first condition in the **pathology** of salivary secretion which merits a short discussion is *increased flow, or salivation*. Since the saliva is swallowed under normal conditions, and we are not conscious of the amount produced, there is great temptation to assume an increased production in conditions in which it flows from the mouth as, for example, in facial palsy; caution is necessary in these cases. True salivation is found in a number of diseases accompanied by intense pain (15) such as trifacial neuralgia, gastric crises, etc. It accompanies inflammatory conditions of the oral cavity and tonsils. It occurs in a whole series of gastric and intestinal diseases (esophageal carcinoma, pyloric stenosis, intestinal parasitism, etc.). Certain poisons produce salivation—mercury, iodine, cocaine on the buccal mucosa, ether, and phenol. Finally, there is a class of substances which acts as true sialogogues such as muscarin, pilocarpin, nicotin, etc. Of these latter, it is known that pilocarpin, physostigmin and muscarin stimulate the autonomic nerve endings, while nicotin acts on their ganglion cells (27). Salivation also occurs in a number of organic and functional diseases of the nervous system. The increased flow of saliva during pregnancy (28) may belong in this category, but the explanation of this condition is in some doubt. So-called "*paralytic secretion*," however, belongs to this group. Destruction of the chorda tympani, or of Jacobson's ganglion has, as an immediate result, complete inhibition of salivary secretion. After the lapse of about

twenty-four hours, the gland again secretes, but continuously (paralytic secretion, Claude Bernard), (36) and this ceases only after complete degeneration of the gland has occurred (30). It is not clear how this is brought about. Langley (31) believes that the central end of the chorda is in a state of increased irritability after section so that it influences the secretion reflexly from the centers. This paralytic salivation is of interest to surgeons because it is often observed in high degree in submaxillary (32) or parotid tumors (33). It may be so annoying that patients "desire operation on account of this symptom" (Kuttner (32)). Thus far, no explanation has been offered for this phenomenon but we may perhaps imagine a destruction of the secretory cranial nerves. [It has also been seen in the gland of the opposite side after hemisection of the cord (Heidenhain).]

Successful attempts to stimulate salivary secretion by chewing paraffin, rubber, etc. are occasionally made for therapeutic reasons, as for instance to mitigate the thirst after operation. It is also believed that pathological transudates of all sorts such as ascites, and hydrothorax may be more quickly absorbed following an outpouring of saliva (34).

*The chemical and physical changes in the saliva during the course of general diseases* have received much less investigation than the quantitative changes, *i.e.*, salivation. There have been large numbers of single observations of the reaction made, however, in all sorts of febrile conditions and in diseases of the abdominal organs. It is often acid (15), (25). Alterations in its enzymic power and in its sulphocyanide content have also been demonstrated, the latter especially in involvement of the chorda in otitis media (35). An attempt has even been made to use the sulphocyanid content as a diagnostic sign in gastric carcinoma, but generally speaking, all these investigations, interesting as they are as single observations or biological facts, do not have any direct practical value at present.

*Diminution or actual absence* of salivary secretion is found in cachectic individuals and in diabetes, cholera, dysentery, etc. presumably on account of the great loss of fluid. Massive loss of blood may also lead to diminished salivary secretion, and furthermore, it is an accompanying symptom in a number of febrile infectious diseases such as typhoid fever and pneumonia (13).

Absence of salivary secretion on the corresponding side, is often observed in middle ear infections if the chorda tympani has become involved in suppuration, or has been disturbed by operation. A case has also been observed of destruction of the salivary nucleus, probably luetic, in which a complete loss of salivary secretion occurred (36). The cases of "*idiopathic asialia*" are especially peculiar, and by no means clear. This condition is occasionally observed in certain psychoses. Buxton

(37) describes a case of absent salivary secretion following mumps, in which a cure was effected by treatment with continuous electric current. X-ray treatment of tuberculous lymph nodes of the neck often leads patients to complain of dryness of the mouth. This is probably due to injury of the substance of the salivary gland which is followed by a diminution of function. In patients, the *results* of considerable diminution, or complete absence of salivary secretion are clear from what has been said regarding the physiological importance of saliva, and do not require detailed enumeration. Subjectively, the principal annoyance is extreme dryness of the mouth, compelling the patient in the instance mentioned by Buxton to moisten every particle of food with water, and making speech almost impossible.

The results of complete loss of salivary secretion have also been studied experimentally (38). All authors are in complete accord in finding that after extirpation of the glands there is a decrease in the amount of gastric juice secreted and in addition, a marasmus which can not be explained merely by the absence of the external secretion of the salivary glands, but seems to require in addition, the assumption that an *internal secretion* is also lacking (39). In dogs, for instance, the lessened secretion of gastric juice after extirpation of the salivary glands did not return to normal, even when the animal was given food which had been well chewed and mixed with saliva by another dog. Improvement was obtained, however, following the transplantation of a salivary gland into the abdominal cavity or after intravenous or intraperitoneal injection of the juice expressed from a normal salivary gland. [This is contradicted by work of Swanson in which he concludes there is no hormone in the salivary glands of dogs which stimulates secretion of gastric juice (40). The rise in acidity which he observed may be due to the absence of alkaline saliva, and the retardation of the maximum secretion rate to absence of the water of the saliva. There must also be a diminished psychic secretion on account of the dryness of the mouth and impaired taste.]

Clinical observations also point to an internal secretory function of the salivary glands (see Buxton's case) and in a manner not yet clear, it seems that there is a certain *correlation with the genital gland* (see Biedl (41)). Such a relation is indicated by the "sympathetic" inflammations of the testes in parotitis, and *vice versa*, by the parotitis frequently observed after ovariectomy. The only remark that can be made in reference to the first mentioned condition, is, that the sympathetic affections of the testes in parotitis have been observed to be more frequent in some epidemics than in others. Every hypothesis for the reason, has failed to be substantiated. It has been stated in the French literature that the pancreas may also be involved in mumps, but the necessary pathological anatomical

investigations are absent (42). [The fact that diabetes mellitus has been known to follow mumps has been cited to show such a relation, but more evidence is necessary for a final decision.]

A disease of great practical importance for the surgeon is **post-operative suppurative parotitis**. It usually appears quite suddenly with high fever, after all kinds of abdominal operations, and is attended with a high mortality (approximately 30 per cent., Wagner (43)). The opinions of authors concerning the route of this infection, *i.e.*, *ascending*—up the larger ducts, or *hematogenous*, are still divided. This is plainly seen in the two newest German references to this subject, which appeared at about the same time, that of Heineke (1) and that of Kuttner (32). The first, after an exhaustive critical review of the literature, comes to the conclusion that only in a few cases of parotitis in typhoid fever, has it been possible to demonstrate a hematogenous source of infection by finding the specific organism in the pus from the gland; while Kuttner on the contrary remarks “that the view of the hematogenous origin of infections of the parotid has again gained considerable ground.”

These diametrically opposed results carried out in simultaneous investigations on the very same subject, become comprehensible when the different viewpoints from which these two authors approached the problem is borne in mind.

Heineke, and with him, many other authors (44), start from anatomical findings, and conclude that positive proof has been brought forth in all the cases in which an histological examination was made, that the first change in suppurative parotitis is the appearance of pus or bacteria in the ducts, and that from these structures the infection is carried secondarily to the other parts of the gland. Thus far, there are only two cases described in the literature in which an anatomical investigation led the authors to assign another route for the infection, *viz.*, through the blood stream. In the one described by Sabrazes and Faguet (45), Stenson's duct was found free of pus, while a lobule of the parotid was completely softened by suppuration. Unfortunately no information of the condition of the ducts in the affected part of the gland is given, so that this case has no real value. A second case observed by Robert, is found cited by Claisse and Dupre (44). The veins within the parotid as well as those in the neck were found full of pus. In this case also, no histological examination was made.

If we, therefore, accept anatomical findings as the basis, we must conclude that suppurative parotitis is *always an ascending infection*. But Rost (46) demonstrated that anatomical findings do not always show what is expected of them. Using dogs, he injected pure cultures of bacteria into the internal maxillary artery which supplies the parotid, and



in the glands extirpated between the third and fourteenth day he found that only the ducts were filled with pus, and that no suppurative thrombosis or embolism had occurred. As injection of the vessel shows, the rapid production of pus in the ducts depends on the very rich blood supply of the salivary glands.

There occurs therefore in the parotid, a suppurative inflammation of the ducts similar to a type found in the kidneys. Orth (47) showed that there is a special form of suppurative nephritis of hematogenous origin which he characterizes as a "simple metastatic suppuration," in which the microorganisms penetrate the walls of the capillary loops of the glomeruli and are carried with the urine to the collecting tubules (nephritis papillaris mycotica).

The decision of hematogenous or ascending infection in a given case of parotitis need therefore not be entirely influenced by the anatomical findings but may be settled by the clinical course alone. There is no difference in the anatomical picture between the ascending and the hematogenous routes of infection.

We may now examine the arguments on which a clinical opinion may be based (48). The first point to consider is that foreign substances are easily excreted by the salivary glands. It must, however, be remarked that there are really only a few substances which are eliminated through this channel; among them are iodine, bromine, mercury, lead and certain alkaloids such as morphine and quinine (27). Furthermore, it has been pointed out that suppurative parotitis occurs in the majority of instances after operations for conditions that are not completely aseptic (1) and the clinical picture of sudden unexpected onset with the high mortality of about 30 per cent. (Wagner (43)) fits in perfectly with sepsis or pyemia. In addition, a large number of the cases which have come to autopsy showed pus foci in other parts of the body (49). It seems forced to explain the very high temperature at the onset of a post-operative parotitis, by the local condition alone.

Formerly, the fact that the disease was found almost exclusively after ovariectomy was looked upon as an important proof of its hematogenous origin. The relation between the genital and salivary glands, which was mentioned by Hippocrates (48) and which, although little understood, finds expression in the orchitis following mumps (50) or the parotitis following contusions of the testicle (51) or in the vicarious swellings of the parotid gland during absent or scanty menstruation, etc. (52), was recognized, and the conclusion drawn that ovariectomy produced vasomotor disturbances in the parotid gland in some manner or other, and reduced its resisting power against infective organisms circulating in the blood. It is at once obvious that the latter part of this conclusion is not

at all necessary. Because even if ovariectomy should cause an injury to the parotid gland, it does not necessarily follow that infection of the parotid must occur by way of the blood stream, and cannot be ascending. After all, post-operative parotitis does not occur relatively so frequently after ovariectomy, because at the time these statistics were compiled, ovariectomy was the most frequent operation in which a laparotomy was performed. This is now changed, and statements of the relation of the antecedent procedure to parotitis at the present time include all kinds of abdominal operations. As already mentioned, it is seen principally after operations in fields not aseptic, *i.e.*, suppurative appendicitis, cholecystitis, gastric operations, etc. (1).

Furthermore, the fact that it is the parotid and only rarely the other salivary glands that are attacked, is hard to reconcile with the view that it is an ascending infection. It is not satisfactory to believe that Stenson's duct occupies a particularly favorable position for the entrance of infection (Hanau 44) since foreign bodies are found much more frequently in the duct of Wharton, and the possibility advanced by Heineke that the mucin content of the saliva from the submaxillary and sublingual glands inhibits the development of pyogenic organisms has up until the present time received no experimental support. On the contrary, according to the newer investigations (see above), it is the parotid saliva which has the strongest bactericidal power. It is, therefore, not clear why the parotid only should become diseased through an ascending infection. The predilection of certain tissues in hematogenous infections is more familiar, even if we cannot explain it. Finally, the fact that suppuration of the parotid often appears very late after an operation also argues against an ascending origin of the infection. It often occurs at a time when this origin cannot be further considered (see below Hallendahl (53)). Furthermore, a suppurative parotitis is almost never observed as a result of stomatitis; indeed in the most common inflammation of the parotid, *viz.*, mumps, an inflammation of the oral cavity is rarely seen, as emphasized by Schottmuller (54).

Nevertheless, the salivary glands are subjected to a number of traumata after and during an operation, and these are quite capable of favoring an infection from within the oral cavity. The first influence is the loss of water, and its resulting diminution of salivary secretion. The patients usually fast before an operation, and they often lose much water by catharsis. After the operation they often receive nothing or very little by mouth, and are dependent on enteroclysis or infusions. Parotitis has also been observed in the course of certain treatments for ulcer, in which very small amounts of water are given and the salivary secretion is diminished (55). The operation itself leads to a diminished salivary secre-

tion. Pawlow (56) has shown experimentally that laparotomy alone, or the pulling forward of a loop of bowel leads to a diminution or complete cessation of secretion, and that which is formed is viscid and turbid. Anesthesia also leads to a diminished secretion (57). A very marked increase is found during the early stages of chloroform anesthesia and it is still more marked with ether. During deep anesthesia, secretion ceases (58), partly on account of the exhaustion from the preceding hypersecretion, and partly also from inhibition of the secretory nerves. All of these factors interacting during the operation, diminish the quantity of saliva for several hours afterwards. Finally, it has been stated that too energetic or unskillful pressure over the parotid during the anesthesia may lead to injury of the gland (Wagner (43)). The infection that follows can naturally occur just as readily through the blood stream as through the ducts. [Opinions in the American and English literature are also fairly evenly divided. Most authors believe that parotitis following operation may be either hematogenous or ascending in origin. Accordingly, operations in septic fields, dehydration of the body, trauma during anesthesia etc. are all recognized and procedures are recommended for prevention on these grounds.]

In addition to suppurative parotitis, the disease picture known as **pneumatocele** should be mentioned. It occurs in glass blowers, and especially in those who blow principally with their cheeks. The entrance of air through Stenson's duct is favored by the flabbiness of the cheeks, the latter of which in addition are often injured by repeated inflammations (59).

Inflammatory changes are also at the basis of **sialolithiasis**, *i.e.*, the formation of salivary calculi. These have been observed in the great majority of cases in the duct of Wharton, and only rarely in Stenson's duct. To understand their mode of formation we must unquestionably call upon the newer physicochemical investigations regarding calculus forming processes in general. According to these, calculi must be considered as "*mixed precipitations of colloids and crystalloids*" (Schade (60)). All the fluids of the body in which calculi form, urine, bile, saliva, etc., are colloidal solutions. Precipitation occurs in such liquids, under the most diversified conditions, the details of which are unknown to us, but broadly, such colloids may be divided into those which are reversibly and those which are irreversibly coagulable. As an example of a reversible coagulation or precipitation in the human body, Schade mentions the uric acid infarcts in the new born, which as is well known, disappear later and leave no trace. Actual calculi, gall stones, urinary and salivary stones belong to the type of irreversible colloidal precipitates. Schade succeeded in imitating such calculus formation in a test tube by adding calcium

phosphate, calcium carbonate or triple phosphates to blood plasma. In the absence of fibrin, for instance, when blood serum instead of plasma was used, the experimental calculus formation did not succeed. It follows that an inflammation of the glands or its ducts must be assumed as a primary cause of the formation of salivary calculi since fibrin is needed. Dal Fabbro (cited by Kroiss) and Kroiss (61) came to the same conclusion on other grounds. Inflammations of the kind that lead to the precipitation of colloids and crystalloids need not necessarily cause a lasting change in the gland. Otherwise it would be inexplicable why there is so seldom a recurrence when the first stone has been removed (1). Furthermore, not every inflammation of the salivary glands leads to the formation of calculi; otherwise parotid calculi would be much more frequent than submaxillary, and the reverse is the case. Either the inflammation must be of a special type, "*a calculus forming catarrh*," or other factors favoring calculus formation in addition to the inflammation must be present. All the theories which have been advanced to explain the formation of salivary calculi might be mentioned here, such as stenosis of the ducts, chronic irritation from pipe smoking (62), entrance of foreign bodies (63), bacteria and so on (see also Kraus (64)), but on the whole, the actual factors operating in the salivary glands are known no better than those in the kidney. Foreign bodies especially leptothrix threads have been found at times, in the center of salivary calculi (65). In such cases, there is a general tendency to assume that these foreign bodies or bacteria are the direct cause of the calculus formation and that they form a nidus of crystallization. A special biological activity of certain bacteria is also mentioned as a possibility. Klebs actually calls such leptothrix threads, lime-algæ, in analogy to those well known to geologists, which form whole mountains by precipitating carbonates from solutions of bicarbonates, and Galippe found hard concretions the scaffolding of which consisted of viable leptothrix threads, in normal saliva which he had kept tightly corked for four and a half years. These experiments are, of course, not conclusive in illuminating the etiology of these calculi, for a saliva saturated with bacteria is certainly not normal after four and a half years. Such a decomposition of saliva as occurs in this experiment cannot take place in the animal body when the saliva has a free means of outflow; also the fact that such concretions in colloidal solutions, preferably form around a foreign body as a center, here represented by fungus threads, proves very little of the origin of those calculi. This behavior is, however, easily explained on physicochemical grounds; precipitates in colloidal solutions "on account of the relatively great surface tension at the phase between foreign body and solution (here saliva) are accumulated at this border" (Schade (60), p. 79).



The primary factor, therefore, is always precipitation in a colloidal solution, which in its turn is dependent on some form of inflammatory process in the gland. Such a foreign body, or bacterium, in the saliva, urine or similar fluid, can never be a crystallization center for reasons which cannot be further discussed here, but which are well known in crystallography. Such salivary calculi produce the so-called *salivary colic* and the "*tumor salivarium*." The latter is a painful swelling of the gland and ducts following the flow of saliva which always results during eating or even at the appearance of food (see above mentioned psychic salivation). Usually the saliva finds its way around the concretion, or it may force the stone out of the duct, and spontaneous cure will result. But the gland may become permanently enlarged by a stone remaining impacted for a considerable time; it then becomes indurated and microscopically shows considerable connective tissue hyperplasia (66).

An *obstruction of long duration* finally leads to complete degeneration of the gland. Occasionally, such a complete obstruction of the duct of Wharton is congenital, and there is found a cystic tumor in the region of the submaxillary gland which corresponds to the dilated ducts. It is interesting that this tumor has been observed immediately after birth which proves that salivary secretion occurs in intrauterine life (67).

The **results of ligation of the salivary ducts** have often been studied experimentally with the view of discovering a method of healing salivary fistulæ in man in a manner similar to that which has long been known to veterinarians (68). Such authors as Viborg, Pelschinsky (66), Rolando (69), Claisse and Dupre (44), Marzocchi and Bizzozero (69), Langemak (66), Kroiss (61) found histologically that ligation of the salivary duct produces, first, a dilatation of the ducts, then an hyperplasia of the connective tissue, perhaps as a result of venous hyperæmia, and finally, necrosis of the parenchyma. Experimentally, this degeneration of the gland takes place without particular inflammatory reaction, but in the few cases in which the duct was ligated in humans with salivary fistulæ, severe inflammation resulted (Hirschfeld (70), von Bramann 3 cases) and this method had to be abandoned. In these cases the procedure must be done of course in pathological and infected tissue.

#### TONGUE, ACTIVE DEGLUTITION, AND ESOPHAGUS

The **tongue** has three functions; it is the organ of taste, it assists in the comminution and propulsion of food, and it is of great importance to speech.

The nerve of *taste* is the glossopharyngeal which supplies the tongue with direct specific taste fibres, especially in the region most sensitive to impressions of taste, the base (circumvallate papillæ), and indirectly

by way of the chorda tympani which travels in the same course as the lingual nerve (71). In the last analysis, however, all taste fibres have their origin in the trifacial nerve, for this function is completely suspended after extirpation of the Gasserian ganglion (72). The tongue receives its motor impulses from the hypoglossal nerve, while its sensory fibres are supplied through the lingual nerve, and in a very small area, by the superior laryngeal nerve. The tongue is the most sensitive part of the oral cavity, especially to thermal and mechanical stimulæ; parts of the oral mucosa, such as the cheeks, perceive changes in temperature to a much less degree (73).

The sense of taste, however, does not depend entirely on the presence of the tongue, but as shown in examinations of patients from whom the organ was completely extirpated on account of malignancy, other parts of the buccal cavity are also supplied with taste receptors. Thiery, and later Ehrmann (74), to whom we owe the most accurate investigations of tongueless men, found that, although their sense of taste was somewhat impaired so that they could not exactly be called "epicures," they nevertheless could taste to a certain extent in the soft palate, the palatine arches, and also perhaps in the posterior pharyngeal wall. Even at present, we do not know of all the points at which taste impressions may be received in the digestive apparatus, and there is, according to Thiery, hardly a place from the red margin of the lips to the stomach itself which has not been at one time or another, considered by physiologists to be involved in this function (75). The diminution following partial destruction of the glossopharyngeal and the lingual nerves, after extirpation of tumors, for example, is naturally more insignificant, and self explained by their anatomical distribution (case of Halban (76)).

While the diminution of taste may be more or less unimportant, the loss of another function—*speech*—may be of much greater import. Even an insignificant wound, or a mild inflammatory process on the tongue, as well as the more serious lesions of the hypoglossal nerve (77), or the hemiatrophy of vertebral caries (78), may cause loss of the distinctness of speech. Speech disturbances are naturally greatest when the whole tongue is removed, or when both hypoglossal nerves are destroyed (77).

Observation of the effects of removal of the tongue were made roughly, even in the earliest time of human history, when tearing and cutting out the tongue were favorite punishments. In our times this mode of punishment is supposedly still practiced in the interior of Persia. It is generally said that these individuals could make themselves understood fairly well, even shortly after the injury, but these statements do not have much scientific value (79). Thiery and Ehrmann have made accurate examinations of patients at various intervals after total extirpation of the tongue,

to discover the type of sounds which could be produced (see also Schulten (80)). They found that among the consonants, the lip sounds were normal, but those which require the tongue are articulated very poorly even a considerable time after the operation. All nasal and friction sounds become very indistinct. An explosion-like "P" is produced instead of a "K" and a "T." No distinction is made between "A" and "AE" or between "O" "OE" and "E." The examples described by Schulten make it clear that these patients can be understood only by those who are accustomed to their speech, and to the alteration in their mode of articulating the consonants.

A slight improvement is noticed if a small thickening of the mucosa develops on the floor of the mouth. This is occasionally produced in an effort to replace the lost organ (Ehrmann). Kettner's observation on a boy four years old, who, in addition to other malformations (cleft palate, etc.), had almost complete absence of the tongue, shows that even with a small portion of the root of the tongue, speech is relatively intelligible (81).

Probably in the olden times, a stump remained when the tongue was torn out, and with its help these miserable people made themselves fairly well understood. Experiences during the war, however, have shown that even a small injury of the tongue, such as an adhesion or the loss of the tip, leads to considerable disturbance of speech.

That function of the tongue which is undoubtedly of the most importance is its share in the act of **deglutition**. Swallowing is an extraordinarily complicated procedure, in which so many muscles take part, that it must be viewed as a whole, without undue emphasis on the part played by the tongue. Numerous investigators in all countries have busied themselves with this problem from ancient times to our own; a multitude of single facts and separate observations have been recorded, and still it cannot be said that the act of deglutition is understood in all its details. Indeed, it has not been sufficiently investigated to satisfy practical surgical needs.

Many authors separate a bucco-pharyngeal phase and an esophago-pharyngeal phase of deglutition, although both blend inseparably into each other (82). If we follow a bolus of food on its way downward (83) we see, as the first preliminary act, a movement of the tongue, beginning with the tip, by which it presses firmly against the hard palate, pushing the food backward toward the pharynx. This action is by no means confined to the muscles of the tongue proper (vertical, longitudinal, transverse), but is shared by others which have their origin and insertion on the hyoid bone, chiefly by the mylohyoides and hyoglossus (84) and also by the geniopharyngeus, genioglossus, and indirectly by the thyrohyoides

which contracts at least a fraction of a second later than the first named muscle. This partially explains the difficulties in swallowing after operations for goiter, although other factors must be considered. This initial movement is important because it gives the bolus an impetus, which alone—at least as Kronecker and Meltzer assume—propels it to the cardiac opening. Schreiber's investigations, however, have added an important point, *viz.*, that the propulsion of food through the esophagus, is, as a rule, assisted by movements of the esophagus itself. Nevertheless, the part played by the tongue and the upper muscles of the neck must be valued quite highly. Meltzer's (85) experiments, furthermore, have shown that experimental section of the nerve to the mylohyoid muscle is sufficient to produce considerable disturbance of deglutition, so that the animal must throw its head backward to permit food to enter the pharynx.

When the bolus has reached the border of the soft palate, the root of the tongue presses against the posterior pharyngeal wall while the soft palate raises itself, and touches the so-called Passavant cushion (formed from the posterior pharyngeal wall), and this closes the pharynx from above. Couvelaire (86) studied the movement of the soft palate in a patient whose nasopharyngeal spaces were exposed after the removal of a carcinoma of the inner canthus. Einthoven has also made similar observations on a living patient (cited by Eykmann (87)).

When the bolus has reached the isthmus of the fauces, lifting of the larynx begins. This is of extreme practical importance. The hyoid bone places itself close under the margin of the inferior maxilla, and chiefly by the contraction of the thyrohyoid muscle, the thyroid cartilage, and with it, the whole larynx, moves closer to the hyoid bone. It may be mentioned briefly that simultaneously with the larynx and the trachea, all those structures connected to them are lifted. This gives us an important point in the diagnosis of adherent tumors, tuberculous lymph nodes, etc. The lifting of the entire larynx upward, and probably somewhat forward, is a protection against choking, inasmuch as the subhyoid fat cushion presses the epiglottis strongly backward and thereby closes the larynx (87). At the same time, probably by a backward bending of the upper part of the larynx (from muscle traction and by the root of the tongue), the epiglottis forms a roof over the opening into the larynx. It is not definitely proved, however, that the glottis is covered completely.

Observations on operated patients (Eykmann), and particularly the India ink experiments of Passavant (88) on man, seem to show that during swallowing, the epiglottis lies on the floor of the upper laryngeal cavity. The latter painted India ink on the rim of the epiglottis and found, after swallowing, imprints on the false vocal cords. The somewhat elementary opinion, formerly prevalent, that the epiglottis acts like a lid and is pushed



into position by the bolus passing over it, must be abandoned on the basis of these later researches. To further ensure closure of the larynx, the glottis contracts simultaneously with the mylohyoid muscles (at the beginning of swallowing), a fact which has been known since Czermak (89) and was recently demonstrated again by the animal experiments of Meltzer. At the same time, or immediately afterwards, the arytenoid cartilages move closer together and bend themselves so strongly downward and forward, that they almost touch the anterior wall of the thyroid cartilage.

A further protection against the entrance of food into the larynx is provided by the interruption of breathing during swallowing (90). A number of observers assume that the centers of deglutition and of respiration are in close relation to each other, partly because of the fact that dyspnea induces swallowing movements (91) but the conditions are not as simple as this, since their observations, for example, water in the stomach of the drowned (see also Cahn (91)) can be explained in other ways. That all these extraordinarily complicated movements designed for the protection of the larynx could be observed when the bolus is in the isthmus of the fauces, may be accepted on the ground of numerous single observations, and differences of opinion exist only as to whether the bolus has already passed downward at the moment when the epiglottis touches the posterior pharyngeal wall. Most authors assume this on the basis of simple theoretical considerations, but Schmid and others believe that the bolus does not pass the opening of the larynx, but slips laterally into the esophagus through the piriform recess. The epiglottis would then adjust itself posteriorly before the bolus slips over it, an occurrence which seems more probable. This explanation appears plausible, especially from the appearance of the upper part of the pharynx from behind (see Spalteholz's Atlas, first edition, third volume, p. 502) and at the same time this would be a good explanation of why needles usually lodge in the piriform sinus. With this, the buccopharyngeal phase, the most important in the act in swallowing, is concluded. The bolus slides into the opening of the esophagus which has been closed during rest, but is now open (92). Before we discuss the next steps, we will consider the *functional impairments* which result from surgical interference, and from those diseases of the tongue of surgical interest.

By excision, or paralysis of the tongue, the act of deglutition can be very seriously impaired. Such a patient usually throws his head backward to enable the food to reach the posterior pharynx (Thiery, Ehrmann). Another disturbing factor also comes into play—the food is less well chewed and mixed with saliva when the tongue is absent, and there is really considerable difficulty in eating larger pieces. When the muscular floor of the mouth can be preserved it offers a certain amount of compensa-

tion, and the cheeks learn to carry on much more extensive movements than in normal individuals. It is therefore advisable to preserve both as much as possible. When the bolus has reached the posterior pharyngeal wall, the patients attempt to bring it past the epiglottis by turning the head. This usually succeeds, although in the absence of the base of the tongue, the epiglottis cannot be closed normally. The other above mentioned mechanism for its closure is, however, still active, so that, even after removal of the whole pharyngeal part of the epiglottis, a dog can drink without choking, provided it can take its time and is not excited (93), (87). Furthermore, Morgagni (94) describes a man at whose autopsy a complete absence of the epiglottis was discovered, and Rosenbaum (95) describes a case in which extirpation of the epiglottis caused no disturbance whatever in swallowing. Therefore, it seems that in man also, the epiglottis may be completely or partially absent without impairment of deglutition (96). The opinion of Schiff that it interposes chiefly between the drops falling from the roof of the palate, the pharyngeal wall and the larynx, after the actual swallowing, has much in its favor.

There is also considerable disturbance in the bucco-pharyngeal phase of swallowing after paralysis of the soft palate (diphtheritic), and in defects in this structure, or in the hard palate, when the closure of the buccal against the nasal cavity is incomplete. For example, in children, with cleft palate, food, especially if fluid, readily flows from the nose. Finally, there are paralyses of the pharyngeal musculature which also lead to interference with swallowing. These occur, for example, during the agony in typhoid fever, in apoplexy, etc., but they have hardly any surgical interest, and need not be discussed. The paralyses of the orbicularis oris muscle in lesions of the facial nerve are worth mentioning, because when the lips cannot close, fluids run out of the mouth. This is also true in the incomplete closure of the mouth in hare-lip, which as is well known, is often accompanied by defects of the palate (cleft palate). In this case, food flows from the mouth and nose, and suckling is interfered with. The same conditions result from wounds, especially war wounds.

The most pronounced disturbances, even complete inability to swallow, are found in fractures or slight injuries (luxations) of the hyoid bone, especially of the great cornua, a fact first pointed out by Valsalva (*Dysphagia Valsalvae* (97)). The importance of this bone in swallowing is shown by the fact that after the injury such patients must be fed with a stomach tube for some time. The prognosis is very grave (about 50 per cent. mortality), and not the least reason for this is the impairment of swallowing, and the danger of pneumonia from food entering the air passages.

The results of section of the mylohyoid muscle or of its nerves, have already been mentioned. It is more serious if the other muscles belonging to this group are also cut, especially the genioglossus, and the geniohyoid. When the middle portion of the lower jaw is resected and the genioglossus is cut, the base of the tongue sinks backward, partly on account of its weight, and partly on account of "spasm" of the antagonists (hyloglossi, styloglossi, stylohyoid). It then covers the entrance to the larynx and serious danger of asphyxia occurs. Since the geniohyoid and mylohyoid will probably also be severed, the hyoid bone loses its support anteriorly, and in its turn increases the respiratory difficulty. These conditions have been studied experimentally by Szymanowsky (98). Similar observations were made in gunshot wounds of the face, and during the war, special bandages were constructed to prevent this backward sinking of the tongue (99).

The act of swallowing has been divided into a bucco-pharyngeal and a pharyngo-esophageal phase. Naturally such a division, like any other in a quickly occurring process, is arbitrary, but it has advantages from the practical standpoint. Physiologically, it is more correct to consider the movement of the bolus by the tongue to the isthmus of the fauces as belonging to the act of mastication. These movements are under the control of the will. But the contraction of the constrictors of the pharynx, the lifting and roofing of the larynx, the movements of the esophagus, etc. are purely reflex, as emphasized by Magendie (100) and as such are exposed to numerous disturbances of importance surgically.

Unfortunately, our knowledge of the *innervation of the esophagus* and the pharynx in man is very imperfect, although it has been increased by the more general use of local anesthesia. We must still, however, rely to a great extent on the facts found by experiment on animals. In the sensory part of the reflex arc are involved, the second branch of the trigeminal, the glossopharyngeal, the superior, and probably the inferior laryngeal nerves. In rabbits, swallowing movements result on touching the soft palate (second branch of the trigeminal) (101), while the glossopharyngeal contains the inhibitory fibres (Kronecker and Meltzer). The former also transmits swallowing reflexes in the monkey, while dogs and cats swallow when the posterior wall of the pharynx is touched (glossopharyngeal). In man, Wassilief could not discover a point on the tongue, palate or pharynx, which when touched, would always produce swallowing movements. Nevertheless he believes the swallowing reflex may be initiated from the sensory region of the pharynx (perhaps the base of the tongue). This is supported by the fact that after cocaineizing this region, swallowing is difficult for about a quarter of an hour. We do not

know, however, the route by which this impulse is transmitted toward the center. Transmission anesthesia might be used successfully in this connection, but at present observations regarding inhibitions in swallowing after anesthesia of the second branch of the trigeminal have not been published, and just as little attention has been given to the glossopharyngeal nerve in relation to these questions (102). Even some time after operation for tuberculous glands of the neck, it has been occasionally observed that the patients easily choke. In the case of goitres which reach far upward it is generally assumed that the superior laryngeal nerve is injured (103) but the cases have not been investigated very carefully thus far.

The epiglottis, the third place from which impulses causing deglutition might be carried centripetally, is supplied on the sensory side by the superior laryngeal nerve. Section in man is done chiefly in tuberculosis of the aryepiglottic fold to abolish the pain in swallowing (lit. see Zencker (104)). No ill effects have been observed after this operation, but such cases are really unsuitable for physiological investigations. The sensory tracts of the esophagus run in the recurrent nerve, but there are also communications with the spinal ganglia (105). According to Zimmermann's investigations (73), the lower portion of the esophagus is insensible to touch and electrical stimuli, while in its upper part it reacts to them. It is insensitive to pressure and temperature differences, and also to some chemicals (alcohol). Other chemicals, such as menthol, are perceived by the sensation of cold, approximately as far as the level of the larynx, but not further along the alimentary tract until it is placed immediately above the anus (106). The motor nerve of the pharynx and esophagus is the vagus, and it carries fibres which cause contraction of the musculature, and others which determine muscle tonicity (107).

In addition to this connection with the brain, the esophagus, similar to the whole intestinal tract, has a second center in sympathetic ganglion cell groups lying in its wall. The innervation is further complicated by the intermingling of the different nerves supplying the various muscle regions (108).

The swallowing center lies in the medulla above the respiratory center, therefore the connection between swallowing and respiration. This briefly described complex reflex arc can be interrupted in any of its parts. We do not know, of course, which separate part of the arc is involved in the individual disturbances of swallowing, but this is not surprising considering our defective knowledge of these tracts in man, especially in the esophagus. Nevertheless some details are known to us. It has been mentioned that cocaineization of the pharynx results in disturbances of deglutition, furthermore, in bulbar paralysis, through destruction of the



center, difficulties in swallowing appear. Explanation and location of the deglutition disturbances (spasm) in tetanus and in rabies offer considerable difficulties (109).

Before we select any of these disturbances for discussion, we must first investigate the normal *part played by the esophagus* during swallowing. Kronecker and Meltzer (84) by the clever expedient of introducing a small balloon into the esophagus to register the movements during swallowing, discovered that the food (chiefly semi-fluid and fluid substances) was projected by contraction of the mylohyoid muscles like a shot to the cardia. This finding was questioned by Schreiber (82), who assigned a much greater importance to the movements of the esophagus in the transportation of the bolus and who, doubtless incorrectly, denied the squirting process completely. As proven by Cannon and Moser (110) by means of x-ray observation, fluids can certainly be squirted directly from the mouth to the cardia. Solid food is carried downward by the musculature, and as Schreiber demonstrated, with differing velocities in the cervical and thoracic regions. This may be correlated with the fact that the cervical part has cross striated, while the thoracic part has smooth musculature. A brief pause in the movement of the bolus occurs at the entrance to the esophagus, and at the cardia.

Meltzer also ascribes a greater importance to the peristalsis of the esophagus in the transportation of the food (111). He found, furthermore, in the dog, the esophagus of which contains only striated muscle, that the upper part is more irritable than the lower. This perhaps explained the differences in the velocity of propulsion in the several parts of the esophagus in this animal. In man, semi-fluids and fluids pass downward entirely from their own weight. When artificial nourishment is needed after operations in the pharyngeal region, it suffices, therefore, to pass a feeding tube through the mouth or nose to the beginning of the esophagus (112). Fluids can be poured into it at will without inciting the movements of swallowing. A fluid enters the stomach without meeting obstruction, since the cardia opens on account of the pressure on its walls. Those cases in which an artificial substitute has been made are of special surgical interest; Kaznelson (113) among others, describes such a case in which a rubber tube reached from the fistula in the neck to a fistula in the stomach. The bolus passed easily through this artificial passage, which leads Kaznelson to believe that the esophagus can be credited with only slight active participation in the transport of food. Schreiber investigated a case of Lexer, in which, using Roux's method, a piece of small intestine was introduced under the skin of the chest to the thoracic aperture (82). The bolus moved downward very slowly, and was always mixed with air. In passing, it might be mentioned that Albert

Wolff (114) observed movements of the axis during swallowing following a traumatic injury.

Great importance has been attached to the so-called narrow places in the esophagus in reference to the location of erosions, the lodgement of foreign bodies, and the development of malignant tumors (lit. see Enderlen (115)). The statements of authors in this connection vary greatly. Thus, Sappey describes only one narrow place; Virchow (116) and others, three; Mehnert, thirteen, but the old teaching of Virchow still has the greatest following. His three narrow places are below the lower rim of the cricoid cartilage; about 2 cm. below the bifurcation of the trachea; and about 2 cm. above the hiatus esophagi. The accurate measurements of Telemann (117) have somewhat altered this teaching. According to him, if the esophagus is opened longitudinally and measured, no narrow places are found. Those described are to be considered as purely functional, occurring partly through unequal contraction of adjacent segments (cardia, hiatus esophagi), and partly through pressure from surrounding structures (bifurcation, cricoid cartilage). The physiological importance of these places, however, is not touched upon in Telemann's work, as we shall see later.

Of the various parts, the *cardia* deserves especial attention. According to Openchowski (118) the centers for its closing are located in the posterior parts of the corpora quadrigemina, and in the anterior columns of the spinal cord. The fibres from the brain are transmitted chiefly through the vagus, and those from the spinal cord mostly through the splanchnics; both end in the plexus of Auerbach. The center for opening lies chiefly in the anterior inferior portion of the caudate nucleus; its fibres also traverse the vagus. Stimulation of the cortex in the region of the crucial sulcus also results in opening of the cardia. That the cardia is closed during rest can be verified at any time by the esophagoscope (112), (119). As the tube approaches, it opens, and the tube can be pushed into the stomach without encountering a strong resistance. Similarly, under normal conditions, the tonic closure of this muscle relaxes automatically when pressure in the lower part of the esophagus reaches a certain degree, whether this pressure is brought about by artificial pumping in of air, or the pouring in of fluids, or by the act of swallowing (v. Mikulicz). This sphincter mechanism is therefore regulated reflexly from the esophagus. Retzius describes the anatomy of this region as follows: there is no annular sphincter (120) but the longitudinal muscle fibres continue into the stomach and close the cardia, not by narrowing of the ring, but by longitudinal contraction (121). There is thus developed, a sort of valve. On the fundus of the stomach, to the left of the esophageal opening, is a fold which also acts as a valve, but its size varies within wide limits.

Finally, fibres from the diaphragm also help in the closure by encircling the esophagus just above its junction with the stomach (122).

**Disturbances** in the nervous innervation lead to the symptom complex known as *cardiospasm*. According to the newer investigations of Fleiner (123), conducted by the x-rays and by stethoscope, the obstruction is not due to the cardiac orifice alone, but the musculature of the gastric sinus is also involved in forming too narrow a channel for the food to pass (see later). This causes the sounds, as heard through the stethoscope, to cover an area from 10 to 15 cm. wider than the region of the cardiac orifice. On the other hand, the operative results of Heller (124) (longitudinal incision of the muscles at the cardia about 3 cm. long), and those of Wendel (124) (longitudinal incision 7 cm. long through the whole cardia and transverse suture), show it must still be accepted that the circumscribed spasm of the cardiac orifice is the most important feature in cardiospasm. Congenital and acquired types are differentiated (125). The clinical symptoms of each are alike. The patients can swallow food; it does not enter the stomach, but remains in the lower part of the esophagus, or in the upper part of the stomach after which it is carried upwards by a strangu-lation which differs from vomiting by the absence of nausea, among other things. The other subjective symptoms, especially pain, differ widely. This may be very severe and some patients feel as though something had been torn in their chests (126). Probably everyone has experienced an uncomfortable sensation from contractions of the esophagus upon a closed cardia after eating or drinking hastily.

The esophagus becomes widely dilated above, and it is usually assumed that this is purely passive from the stasis of food. In most cases, however, it is more probably due to atony of part of the esophagus coincident with the cardiospasm. It was formerly considered as the primary factor (Stark (127), Rosenheim (119)) probably because at autopsy, the dilatation of the esophagus was found (Vormagen, Fleiner (126)) when naturally the spasm could no longer be demonstrated. Another fact which seems to support a nervous origin is that high grade dilatations such as are seen in cardiospasm are seldom met in organic obstructions from strictures or from stenosing carcinomata even when located near the cardia (151) (Gottstein (119), p. 111). Food can often be forced mechanically through the orifice if it is lying at the cardia (128). Kraus (129) found both vagi diseased in a case with marked dilatation. Similar cases are described by Paltauf and Heyrowsky (130) in which other symptoms due to the vagus had been observed clinically. Thus Kaufmann described a case in which the pulse rate sank to 40 beats a minute on those days when the cardiospasm was especially pronounced, and in which the vagus irritation was considerably relieved by atropin (131).

Experimentally, Krehl (132) observed paralysis and dilatation after section of the vagus nerves in the neck. When the section is made below the hilus of the lungs, no effect is demonstrable either on the cardiac orifice or on the esophagus (133), (122).

On the other hand, the investigations of Kronecker and Meltzer, Schiff, A. Bernard, Sinnhuber (134), and others have shown that after section of the vagi in the neck, the cardiac orifice goes into a state of contraction and remains hardened for days, on account of the independent action of the sympathetic ganglion cells lying in its walls. It is only later that it becomes paralyzed and dilates, as the studies of Krehl have shown. Cardiospasm with secondary dilatation of the esophagus is therefore to be considered as a vago-paralytic process (129), or as in the case of Kaufmann-Kienbock (131) as a result of vagus irritation. The particular part of the nervous system in which these changes have their primary site is unknown, but it probably differs in the various individual cases. The observations of Goltz (107) who saw a lasting spasm of the esophagus in the frog not only after section of both vagi, but also after destruction of the medulla oblongata, probably indicate that the affection may also be brought about by cerebral conditions. In many cases, it is probably not to be expected that gross changes in the nerves will be found, at least this thought is supported by the fact that prompt relief can often be obtained by a single energetic stretching of the musculature (Gottstein, Wilms, and others). In others there is an increased irritability of the vagus as a whole (vagotony), in which spasms of parts of the intestines are also present (135). In such a case, the cardiospasm must be classed as a constitutional disease.

It should be mentioned in passing, that according to the summaries of Widmer, Tilmann, Reich (136) and others, unilateral section of the vagus in the neck in man, results, with the exception of permanent injury to the recurrent nerve, in nothing but a quickly subsiding acceleration of the pulse. Pulling or stretching, *i.e.*, irritations of the vagus, are, however, extremely dangerous and have often caused death. This danger may be avoided by previous cocainization (137).

In addition to this combination of flaccid paralysis of the esophagus with contraction of the cardia, *localized paralyses* of isolated parts above the cardia are also found. Complete paralyses occur in bulbar-palsy, multiple sclerosis, and similar affections of the central nervous system, usually, however, in the terminal stage. Gottstein (119) has described a post-diphtheritic paresis of the esophagus, *i.e.*, paralysis following disease of the peripheral nerves. A weakening of the esophageal musculature and not a complete paralysis, is spoken of as "atony." It occurs usually, as a part of a general atony of the entire body and can be diagnosed with



certainly only by  $x$ -ray examination (138). Small quantities of soft food are transported very poorly; they are spread over the walls of the organ and remain there for some time. The cause of this atony is as little known as the underlying anatomical basis.

In addition to the dysphagias from paralyses, there is also a spasmodic dysphagia in the upper parts of the esophagus (139). The anatomical data, briefly sketched above and the findings of Goltz, who observed reflex contractions of the esophagus in frogs, after irritation of the esophageal wall or of the sciatic nerve, are of value in understanding these conditions. Unfortunately no corresponding investigations seem to have been made in larger warm blooded animals. Our clinical experiences, however, especially with spasms in inflammations of the esophagus, and in the irritations of foreign bodies, etc. support the view that those spasms, particularly in the more central parts of the esophagus are reflex processes, incited by peripheral irritations of various kinds. The spasms in swallowing observed in the hysterical have thus far not been explained very adequately.

[In a consideration of all these processes, *i.e.*, swallowing movements of the esophagus, cardiospasm, etc. it must be borne in mind that the vagus nerve about which much of these mechanisms center, probably carries in man not only motor but also inhibitory fibres. There is great variation in the response in different species of animals as well as in the relative proportion of smooth to striated muscle. This makes the drawing of analogies precarious. Smooth muscle will contain Auerbach's plexus and other local ganglia while in striated muscle they will be absent. The inhibitory control of the vagus seems to obtain in primitive types, and as Carlson and Luckhardt suggest, if this predominates in a species, cardiospasm could be produced not by "vagotonia" but by vagus "hypotonia."]

Spasms at the entrance to the esophagus are of particular importance. Killian (92) described a special ring of muscle in that part of the constrictor pharyngis (*M. fundiformis*), which, like the cardia, is said to be closed during rest, while the remainder of the esophagus is an open, air filled tube (*v.* Mikulicz (112), Sauerbruch (140). Killian considers that spasms at this entrance may be the primary cause of so-called pulsion diverticula (141). They often offer great difficulties to the introduction of food.

These diverticula, also called *Zenker's diverticula* (142) are "sac-like outpouchings of the posterior or lateral esophageal walls at the junction of the pharynx and esophagus, caused, or further developed, by continuous pressure from within" (143). Explanation of their development has always been difficult. They have been considered as malformations, or as related to the branchial clefts, or as indicating an atavistic tendency (*e.g.*, the mouth pocket in the pig), but all these theories have very little

corroborative material in embryological facts (143). For these reasons, the old Zenker-v. Ziemssen idea of a purely mechanical origin still has its place. "A circumscribed area of the wall of the esophagus loses its resistance because of a localized injury to its supporting muscle fibres, and gives way from pressure acting from within during swallowing" (Zenker, V. Ziemssen (142), p. 58). We actually know from the normal anatomy, that there is such a weak place in the posterior wall at the esophageo-pharyngeal junction, for Laimer (144) has described a three cornered space in which the longitudinal muscle fibres are lacking, and it is these latter which, on the whole, are considered the most important support for the pharynx and esophagus.

That this weak place should be bulged by the pressure of a large bolus swallowed with particular force, especially when the entrance to the esophagus is spasmodically closed, seems rational (this assumption had been made by Monro in 1811 (144) and, as additional evidence this place has been found to have the least elasticity (143)). But this theory is not generally recognized, even though it does explain the causal relations fairly well. The lateral diverticulæ, especially those situated at the entrance to the esophagus, are regarded by many as remnants of branchial clefts (145) although in the embryonal life of man, the branchial clefts never extend downward this far. Further investigations are necessary in this field, especially directed toward discovering whether the diverticulæ have muscular layers, a point on which v. Bergmann lays special stress, and whether there is some lesion in the nerves. It is quite conceivable, though not shown thus far, that above the spastically contracted esophageal entrance, an atony of individual muscle bundles with eventual degeneration of the nerve elements, similar to that occurring in cardiospasm, is present.

There are, however, true *congenital diverticulæ*. These are situated higher than the Zenker diverticulæ, *i.e.*, in the pharynx itself, and are derived from an internal incomplete fistula of the neck.

There are also pulsion diverticuli in other parts of the esophagus, situated almost exclusively on the anterior wall, either directly above the cardia (epicardial), or above the left bronchus (epibronchial). Some of these structures must certainly have originated from traction, and their enlargement is due to pressure of the food trapped in them (traction-pulsion diverticuli) (Stark). Others may be considered congenital, arising during the division of the early common intestino-respiratory tube, by the pulling outward of bands of adhesions attached to the esophagus. Weak places may also be acquired through inflammatory ulceration, pressure ulcer, etc. (see later). These have, so far, not been described as a cause of pulsion diverticuli in the middle section of the esophagus, but

it has been frequently asserted that these diverticuli are often exciting causes of spastic spasms of the musculature, another statement without definite proof (146).

Most of those found at autopsy, often accidentally, are traction diverticuli of the middle and lower esophagus formed by the pull of adherent lymph nodes sclerosed by anthracosis and fibrous tissue. These may occur without symptoms. They often, however, break through into adjacent tissue and lead to very grave clinical conditions, such as mediastinitis, esophageo-tracheal fistulæ, etc. In addition to the disturbances in the motility of the esophagus, there are also *sensory disturbances*. As the investigations of Zimmermann show, the lower part of the esophagus is insensitive to touch and electrical stimuli, while the upper part feels them (73). It is sensitive throughout its whole length to pressure and temperature, to concentrated alcohol, but not to 1 per cent. hydrochloric acid. Anesthesia and hyperesthesia have been repeatedly observed during esophagoscopy in hysterical individuals (Gottstein (119)). But more accurate examinations of the sensory conditions, such as Rosenheim tried to make on his patients, have thus far lead to no results. We do not know if the sensitivities of the esophagus suffer in diseases of the central nervous system.

*Organic stenosis* is less difficult to understand physiologically than nervous spasm and dilatation. These stenoses may be divided into those due to disease of the esophagus itself, *i.e.*, stricture *per se*, and those caused by pressure from without. This latter condition is sometimes observed in strumous patients. The true strictures result chiefly from caustics. Their usual situation is at the "three narrow places" described above, *viz.*, at the entrance to the esophagus, opposite the bifurcation of the trachea, or at the cardia. The latter are often quite extensive, and lead to later tubular constrictions which often reach far upward. This is explained by the act of normal deglutition described above, as demonstrated, particularly by Telemann by his comparison of the deglutition curve of Schreiber with Zenker's corrosion curve (117). The irritation of the caustic produces a coincident cardiospasm by which the fluid is held for considerable time in the cardia (von Mikulicz (112)). Above the stricture, an hypertrophy of the musculature develops, with dilatation, the latter, however, of not very high grade. This combination of dilatation and hypertrophy reaches to the narrowest part of the stricture, as is easily understood, so that the change from dilatation to constriction is quite sudden. This is the reason that it is often very difficult to introduce a bougie from above, while it is easy to find the narrowest place from below. In the absence of dilatation, the stricture opens downward gradually like a funnel, in which case there is great danger of forcing a false passage

from above. As von Hacker (147) has shown, perforations at the level of the bifurcation occur always on the left side of the wall of the esophagus, because at that point it turns to the right. Conversely, a perforation above the cardia is usually situated on the right side of the wall, since it turns to the left as it passes through the diaphragm.

Congenital stenosis or complete absence of part of the esophagus cannot be discussed here. They are easily explained on embryological grounds (148).

That the esophagus, which is exposed to the most varied kinds of thermic, chemical, bacterial, and mechanical irritations is also, at times, the seat of inflammation, is not astonishing, but because of the excellent protection offered by the lining epithelium, these inflammations are relatively rare. Surgically, it is important that spasms which lead to disturbances of deglutition can be incited by catarrhal conditions, difficult to explain without esophagoscopy. It is also important to remember that during the course of scarlet fever (149), and other infectious diseases deep ulcerations may appear, and lead secondarily to strictures. The most serious of the diffuse inflammations is a phlegmon, which, except when it follows the presence of a foreign body, corresponds to phlegmonous gastritis. Its origin is as little understood as the origin of the latter condition.

*Circumscribed ulcers* are also infrequent. The luetic, actinomycotic and the tuberculous types may be mentioned. The latter have recently been described. It is not known with any degree of certainty whether they are produced by the entrance of tubercle bacilli from the blood, or by local invasion (150). They often cause extensive loss of tissue, which, however, causes remarkably little discomfort.

Pressure ulcers form a special group. These also appear by preference at the three physiological contractions, where as already stated, the walls have the least elasticity. Thus Kermauner (151) has described cases in which permanent sounds have caused extensive necrosis at the hiatus, bifurcation, and cardia. Such ulcers form during the agonal period, especially at the level of the cricoid cartilage, when the larynx sinks backward and presses against the spinal column. Pressure necroses appear also when tumors or tumor-like growths press on the organ from without. The most varied things, such as aneurisms, tuberculous glands, varices, etc. have been described. The most dangerous, in this respect, are the exostoses of the vertebral column (152). We know, therefore, of a great variety of external factors which cause ulceration, but we do not know why the necroses occur at these particular points, or why the esophagus, with its great elasticity, is attacked at all by pressure ulcers. Perhaps investigations of the blood vessel distribution may be helpful.



The peptic ulcer is a much debated affection of the esophagus. Even in the comprehensive work on the diseases of this organ by Zenker and von Ziemssen, their occurrence is disputed. Recently, however, a series of about sixteen undoubted cases have been observed and described (compiled by Kappis (153)). A number of the patients had, in addition, ulcers in the stomach or in the duodenum, which indicates a correlation. Regarding the etiology, of which we know very little, it may be worth mentioning that islands of gastric mucous membrane were found in the esophageal lining in some cases, making it possible that the peptic ferment necessary for the formation of the ulcer, came directly from the esophagus itself, and not, as in most other cases, from regurgitated gastric contents. Vomiting alone cannot, of course, ever be a cause; other additional influences of which we know very little in detail are needed (see gastric ulcer). Toxic injuries can be excluded, for there is found, as Rost has described (154), in the vomiting and injury of the esophagus from toxemia (peritonitis), a severe edema, but no ulceration.

During impairment of the circulation, particularly during the agonal period, the digestive action of the vomitus or of the back flowing gastric contents through an open cardia, has been held responsible for the development of *esophagomalacia*, and the quite frequent rupture.

The present view in this latter, much debated question, is that such a softening may actually take place, but only during the agonal period. Vomiting may then lead to rupture (Zenker, von Ziemssen (142), Cohn (155)), but a spontaneously appearing esophagomalacia such as was supposed to occasionally occur in healthy persons, has not been observed beyond question. Sudden rupture during vomiting must therefore be explained on other grounds. According to the compilation of Cohn, this condition occurs almost exclusively in middle aged men who are heavy drinkers. The rupture as found, is usually a longitudinal tear, and is typical of rupture from excessive pressure within. This can be easily imitated by closing a rubber tube at one end and attaching the open end to a water faucet; when the pressure is turned on, the tube will tear longitudinally at a given moment (156). In the esophagus, the question resolves itself to these points—does the rupture occur because the internal pressure becomes too high during the vomiting, or, as has been assumed, from kinking or contortion of the organ after pleurisy; or from the presence of a strong broncho-esophageal muscle; does a certain muscle segment go into spastic contraction, etc. or does it occur under normal pressure in an organ with abnormally weak walls? Thinning has often been described, and usually follows ulcerative, sclerotic, or arteriosclerotic processes. Brosch has measured the strength of the wall of a normal esophagus and found that there are considerable differences in the thickness of different seg-

ments. A thin strip is often found anteriorly in the region of the trachea. Furthermore, it is known that the strong musculature of the esophagus can slide under the mucosa to a considerable extent. For this reason, during esophagotomies, the incised area must be fixed at once with loops of thread to keep the edges separated, otherwise the musculature slips over the hole in the mucosa (147). It is quite conceivable that an area in the esophagus, otherwise normal, can momentarily be made thin through such a displacement of the muscularis. Roy (152) describes a case of rupture in which an exostosis of the thoracic vertebral column produced a demonstrable thinning of the wall. Both possibilities of sudden tearing, therefore, are quite conceivable, but it would seem in the case of a transverse tear, that the conception of a weak place in the wall is more logical (see Cohn's list), while in a longitudinal tear, in which no microscopical changes in the torn place are demonstrable, the logical cause is a suddenly increased internal pressure (see Petren and V. Lichtenberg (157)).

In closing this chapter, attention might be called to a peculiar anomaly in the course of the right subclavian artery which leads to a difficulty in deglutition, often extremely difficult of differential diagnosis. This artery may arise from the left side of the arch of the aorta, and may turn to the right between the esophagus and vertebral column, or between the esophagus and the trachea, and thereby cause disturbances to the trachea or esophagus, or both. Girard and Mouton (158) have recently reported two such cases of dysphagia and dyspnea lusoria.

#### LITERATURE TO SALIVARY GLANDS AND ESOPHAGUS

1. Heinecke: Deutsch. Chirurg., 1913, 33. Notnagel's Handbuch, 16, part 1. For lit. see Kraus.
2. Ludwig: Wiener med. Wchscht., 1860; 31st Naturforscherversam., 1856; Ztschr. f. rat. med., 1851.
3. Heidenhain: Pfluger's Archiv., 1872, V. 5, p. 309.
4. Kohnstamm: Anat. Anzeigen, 1902, 21, 362.
5. Leriche, R.: Zentblatt f. Chirurg., 1914, No. 41, 754. "Behandlung der permanenten Parotisfisteln durch die Entnervung der Speicheldrüse."
6. Trönyl: Zentralbl. f. Chir., 1917, No. 48.
7. Rost: Lehrbuch der Kriegschirurgie Borchard-Schmieden, 1920, 2 Ed. "Gesicht v. Mundhöhle."
8. Gaultier, R.: "Le syndrome œsophago-salivaire de Roger dans le cancer de l'œsophage," Arch. des. malad. l'appareil digestif, 1909, Bk. 3, 590-606.
9. Pawlow: Ergeb. der. Physiol., 1904, 3-1, pp. 177-184.
10. Brunnacci: Arch. de Fisiol., 8.
11. Popielski, L.: "Ueber die Gesetze der Speicheldrüsentaätigkeit," Pfluger's Archiv., 1909, 127, 443.
12. Jappeli, G.: "Untersuchungen über die Speichelabsonderung 2. Speichelvarietäten und Einfluss des Reizungsortes auf die physikochemischen Eigenschaften des Unterkieferspeichels," Ztschr. f. Biol., 1908, 51, 42 and 127.



13. Jawein: Wiener med. Presse, 1892, 15.
14. Jappeli: "Über die physico-chemischen Bedingungen der Speichelabsonderung," Ztschr. f. Biol., 1906, 43, 398.
15. Fleckseder: "Der gemischte speichel des Menschen, sein normales verhalten und seine Veränderungen in Krankheiten," Ztschr. f. Heilkunde, 1906-27 (abstr. M. S. 231) (lit.).
16. Hofbauer, L.: "Tägliche Schwankungen der Eigenschaften des Speichels," Pflüger's Archiv., 1897, 65, 503. Chittenden, Richards, Am. J. Physiol., 1898, 1, 462.
17. Florain, L.: "Essai sur la salive Humaine et sur les propriétés physiologiques du sulfocyanate de potassium," Gaz. med. de Paris, 1899, 7, 6, 317.
18. Sanarelli, G.: Centralblatt f. Bact., 1891, 10, 817. Clairmont, P.: Wiener klin. Wchschr., 1906, p. 1397.
19. Grawitz, E. and Steffen, W.: "Die Bedeutung des Speichels und Auswurfs für die Biologie einiger Bakterien," Berlin Klin. Wchschr., 1894, 31, 419.
20. Elinger: Deutsche med. Wchschr., 1895, 381.
21. Wehrmann, C.: "Contribution à l'étude du venim des serpents," Annales Past. Inst., 1898, 12, 510.
22. Carrière: Annales Past. Inst., 1899, 435. Carrière, G.: "Due sort de la Toxine tetan. introduite dans le tube digestif des animaux," Comp. r. soc. Biol., 1899, 51, 179.
23. Gottlieb and Sicher: 85th Naturforscherversammlung, Wien, 1913.
24. Luciani: Trans. by Frances Welby. Human Physiol., MacMillan, 1913, V. 2, p. 158.
25. Salkowski, E.: "Zur Kenntniss pathologischen Speichels," Virchow's Archiv., 1887, 109, 358.
26. Biernacki, E.: "Die Bedeutung der Mundverdauung und des Mundspeichels für die Tätigkeit gesunden und Kranken Magens," Ztschr. f. Klin. Med., 1892, 21, 97-117.
27. Mayer Gottlieb: Die Experimentelle Pharmacologie, 1910, p. 141.
28. Schramm: Berliner klin. Wchschr., 1886, Dec.
29. Bernard, Claude: Journ. de l'anat et de la Physiol., 1864, 507.
30. Maximoro: Zentralb. f. Physiol., 1900, 249. "Die Veränderungen d. Speicheldrüsen nach durchtrennung der chorda Tympani."
31. Langley: J. Physiol., V. 6, p. 71.
32. Kuttner: Handbuch d. prakt. chir., V. 1, p. 743 and 718.
33. Rost: Personal observation.
34. Leube: Festschr. z. 50 j. Bestehend. Würzburger phys. med. Ges., 1899.
35. Alexander and Reko: Wiener klin. Wochschr., 1902, 1089.
36. Zagari: "Policlinico," 1907, Feb. Cited in Ztrblatt f. inn. Med., 1907, p. 473.
37. Bunton, A. St.: "Complete suppression of saliva after mumps," Lancet, 1883, 1, 1087.
38. Hemmeter, J. C.: "Die Wirkung der Total extirpation sämtlicher Speicheldrüsen auf die sekretorische des Magens beim Hunde," Biochem. Ztschr., 1908, 11, 238. Morano, G. P. and Baccarani, U.: Cited in Zentralbl. f. Chir., 1902. "Sugli effetti dell'asportazione delle glandole parotidi e sotto-mascolari nei coniglio. Milano, F. Vallardi, 1901-12.
39. Mohr.: Ztschr. f. Geb. and Gynak., 1913, 408.
41. Biedl (Artur): "Die Innere Sekretion," 3 Ed. Urban and Swarzenberg, 1916. "Ihre physiologischen Grundlagen und ihre Bedeutung für die Pathologie."

42. Auch: Journ. de med. de Bordeaux, 1905, 44. Guerin: Journ. de med. de Bordeaux, No. 49, 1905, No. 44, 1908-38.
43. Wagner: Wiener Klin. Wchschrft., 1904, p. 1414.
44. Hanau, A.: "Ueber die Entstehung der eiterigen Entzündung der Speicheldrüsen," Ziegler's Beiträge, 1889, 4, 48, p. 7. Nicol: "Ueber genuine eitrige Parotitis," Ziegler's Beiträge, 1912, 54, p. 385. Muller: Inaug. Diss. Halle, 1883, p. 26. Claisse, P. and Dupre, E.: "Les infectious salivaires," Arch. de med. exp., 1894, 6, 41 and 250. Dittrich, P.: "Über einen Fall von eitriger Parotitis und deren etwaigen Zusammenhang mit äusseren Verletzungen," (Prag.) Ztschrft. f. Heilkunde, 1891, 12, 269-280. Wendt, E. C.: "A contribution to pathological histology of acute parotitis," N. Y. Med. Journ., 1880, 32, 248. Virchow: Alte Charité Annales., 1858-8, 3rd. half.
45. Sabrazes, J. and Faguet, C.: "Infection puerperale staphylococcigul, pelva peritonitie, endocardite, ulcers-vegetante, parotidite suppuree d'origine embolique," Gaz. des Hop., 1894, 67, 1039, 41.
46. Rost, F.: "Experimentelle Untersuchungen über eitrige Parotitis," Deutsch. Ztsch. f. Chir., 1914, 130, 305.
47. Orth: Lehr. d. spez. path. Anat., 1889, 2, 64. Orth: Nachr. v. d. kgl. Ges. d. Wissensch, Göttingen, 1895, p. 19.
48. Hellendahl: Med. klin., 1908, 452. Moricke: Ztschft. f. geb. u. Gynak., 1880, 5, 348. Ruttermann: Inaug. Diss. Berlin., 1893. Bumm: "Über parotitis nach Ovariectomie," Munch. Med. Wchsft., 1887, 36, 173.
49. Levy, R.: "Discussion on post. op. parotitis," Berlin. klin. Wchschrft., 1912, 49-1, 765.
50. Herb, E.: "The combination of these diseases has also been shown experimentally by Herb," Zentralblatt f. innere Med., 1900.
51. Billroth. Cited in Wagner (43).
52. Mohr: Versam. des deutsch. Ges. f. Gyn. Halle, 1913. Krapp: Phila. Med. Times, 1879.
53. Hallendahl: Med. kliniks., 1908, 452.
54. Schottmüller: "Parotitis epidemica," Notnagel's spez. Path. u. Therap., 1904, 3, p. 37.
55. Gaultier: Archiv. des. malad. l'appar. digestiv., 1910.
56. Parolon: Pflüger's Archiv., 1878, 12, 272.
57. Berth: "Über parotitis nach gynak. operation," Inaug. Diss. Greifswald, 1886.
58. Buttermann: "Parotitis nach Ovariectomie," Inaug. Diss. Berlin, 1893.
59. Narath: Deutsch. Ztschr. f. Chirur., 1912, 119, 201.
60. Schade: Munch. med. Wchnsft., 1909, 142 and Med. kliniks., 1911, 565.
61. Kroiss: Bruns Beiträge, 1905, 47, 470.
62. Haurel: Wiener klin. Wchnsft., 1900, 163.
63. Auerbach: Jahrbuch f. Kinderheilkunde, 1910, 22, 213.
64. Krauss: Nothnagel's Handbuch, 16, 1 part 1st. half.
65. Galippe: Compt. rend de seanc. de l'acad., 1893, No. 19. Klebs: Archiv. f. exp. Path., 1876, 5, 350 and 365. Alexandre: Rev. de Chir., 1906, 1, 732.
66. Langemak: Virchow's Archiv., 1904, 175, 299.
67. Sultan: Deutsche Ztschrft. f. Chir., 1898, 48, 133.
68. Viborg: Virchow's Archiv., 1904, 175, 299.
69. Marzocchi and Bizzozero: Centrbl. f. Chirurg., 1903, 1295. Rolando: Zentralblatt f. Chir., 1899, 985.
70. Hirschfeld: Inaug. Dissert., Berlin, 1889-1890.

71. See Corning: "Topographical Anatomy, 1911, 3rd edition.
72. Bircher: Deutsch. Ztschft. f. Chir., V. 109.
73. Zimmermann: Mitt. a. d. Grenzgebiet., 1909, 20, 454.
74. Ehrmann: "Funktionsstörungen an Geschmacksin Sprache, und Schluckbewegungen nach Totalexstirpation der Zunge," Bruns Beiträge, 1894, 11, 595. Thiery: "Untersuchungen über d. Geschmacksempfindungen usw. eines Zungenlosen," Arch. f. klin. Chir., 1885, 32, 414.
75. See also Giesoro and Hahn: "Ueber Geschmacksempfindungen im Kehlkoß," Ztschr. f. Physiol. and Psychol. d. Sinnessorgane, 1902, 27.
76. Halban: "Zur Physiol. d. Zungennerven," Wien. klin. Rundschau, 1896, No. 4.
77. Deutsch. Chir., 34, No. 132.
78. Ranzier: Montpellier med., 1913, V. 36.
79. Bronadel: Annales d'Hygien, 1904, refer. to Zentralblt. f. Chir., 1904, p. 1167.
80. Shulten: Deutsch. Ztschft. f. Chir., 1893, 35, 417.
81. See Zentralbl. f. Chir., 1907, p. 193. Also Weil in Maschkas; Handbuch d. Gerichtlichen Medizin, 1881, V. 1, p. 258, who observed a patient operated by Billroth for carcinoma of the tongue. He could articulate fluently even though but a small part of the tongue had been left remaining.
82. Schreiber: "Ueber den Schluckmechanismus," Arch. f. exp. Path. u. Pharm., 1901, 46, 446; also Arch. f. exp. Path. u. Pharm., 1911, 67, 72; Grenzgebiet, V. 24, p. 35.
83. Scheier: "Zur Verwertung der Rontgenstrahlen f. d. Physiol. des Schluckactes," Fortschritt auf. d. Gebiet d. Rontgenstrahlen, 1911-12, 18, 377.
84. Kronecker and Meltzer: "Der Schluckmechanismus, seine Erregung und Hemmung," Arch. f. Anat. u. Physiol., 1882-1883, suppl., p. 328.
85. Meltzer: Arch. f. Anat. u. Physiol., 1880, p. 296.
86. Couvelaire: "Sur le rote du voile du palais pendant la deglutition, etc.," Journ. de Physiol., 2, p. 280.
87. Eykmann: "Sitzungsbericht Akad. Wissenschaft," Wien. klin. part 3, 1891.
88. Passavant: Virchow's Arch., 104, p. 444.
89. Czermak: Collected Writings, V. 6, p. 2.
90. Marckwald: Ztschft. f. Biol., N. F., 1889, V. 7.
91. Schwartz, Cahn, Duccesi: Zentralbl. f. Physiol., 1905, 19, 995.
92. Killian: Munch. Med. Wchschrft., 1907 and 1908, No. 34.
93. Magendie Longet: "Lecons sur la physiologie de la digestion, 1868, 13th lesson.
94. Morgagni: "De sedibus et caus. morborum," 1761, Book 3, No. 13, Venedig.
95. Rosenbaum: Arch. f. klin. Chir., 1894, 49, 773.
96. Schmidt: "Die Krankheiten des oberen Luftwege," 1894, p. 44.
97. Albert: Lehrbuch d. Chirurgie, 1881, V. 1, p. 425.
98. Szymanowsky: Cited by König in Lehrb. d. Chirurg. 2 ed., 1878, p. 304.
99. Rost: Gesicht u. Mundverletzungen in Borchard-Schmieden Lehrbuch d. Kriegschirurgie, 2nd edition.
100. Magendie, cited in Luciani: Human Physiol., V. 11, p. 143.
101. Kahn: Arch. f. Anat. u. Physiol., 1903, p. 386.
102. Hirschel: Munch. med. Wchschrft., 1912, 2.
103. v. Eiselberg: In Handbuch d. prakt. Chir., 4th ed., 1913, V. 2, p. 386.
104. Zencker: Munch. med. Wchschrft., 1919, p. 1167.
105. Luscher: Ztschft. f. Biol., 1897, V. 35. de Witt: Journ. of comp. Neurol., 1900, 10, 382.
106. Schwenkenbecher: Munch. Med. Wchschrft., 1908, No. 28.

107. Goltz: Pfluger's Arch., 1872, V. 6, 616.
108. Kahn: Arch. f. Anat. u. Physiol., 1906, p. 355.
109. Rose: Deutsch. Chir., V. 8.
110. Cannon and Moser: Am. J. Physiol., 1898, 1, 435.
111. Meltzer: Zentralbl. f. Physiol., 1907, 21, 94 and 70.
112. v. Mikulicz: Mitt. aus d. Grenzgebiet, 1903, 12, 509.
113. Kaznelson: Pfluger's Archiv., 1907, 118, 327.
114. Wolff, A.: Berlin. klin. Wchschrft., 1918, p. 422.
115. v. Hacker: Handbuch d. Chirurg., 4th ed., V. 2, p. 13. Lit. see Enderlen: Deutsch. Ztschrft. f. Chir., V. 61.
116. Virchow: Virchow's Arch., 1883, V. 2.
117. Telemann: Dissert. Konigsberg, 1906.
118. v. Openchowski: Arch. f. Anat. u. Physiol., 1889, p. 551.
119. Gottstein: Mitt. aus. d. Grenzgebiet, 1899-1901, V. 6 and 8. Rosenheim: Deutsch. Med. Wchschrft., 1895, No. 45.
120. Retzius: Cited by Fleiner Naturhist. med. Verein Heidelberg, 1919.
121. Kelling: Arch. f. klin. Chir., V. 64, p. 402.
122. Sauerbruch and Haecker: Deutsch. med. Wchschrft., 1906, No. 31.
123. Fleiner: Munch. med. Wchschrft., 1919.
124. Heller: Mitt. a.d. Grenzgebiet, V. 27. Wendel: Verh. d. Deutsch. Ges. f. Chir., 1910.
125. Fleiner: Munch. med. Wchschrft., 1910; p. 982.
126. Fleiner: Munch. med. Wchschrft., 1900.
127. Stark: "Die diffuse Erweiterung der Speiserohre," Deutsch. Praxis, 1903, Munchen.
128. Obemdorffer: See Munch. med. Wchschrft., 1911, p. 1988. Dietler: Ztschrft. f. Rontgenkunde, 1912, 14, No. 9.
129. Kraus: Festschr. f. Leyden, 1902, V. 1.
130. Heyrowsky: Wien. klin. Wchschrft., 1912. Paltauf: Wien. klin. Wchschrft., 1908.
131. Kaufmann: Wien. klin. Wchschrft., 1908 and 1909.
132. Krehl: Arch. f. Anat. u. Physiol., 1892, suppl. p. 278.
133. Stark: Munch. med. Wchschrft., 1904.
134. Sinnhuber: Ztschrft. f. klin. Med., V. 50. Bernard, A.: Cited by Kraus.
135. Neugebauer: Wien. klin. Wchschrft., 1914. Wilms: Deutsch. Ztschrft. f. Chir., V. 144.
136. Reich: Brun's Beitrage, V. 56. Widmer: Deutsch. Ztschrft. f. Chirurg., V. 36. Tillmann: Deutsch. Ztschrft. f. Chir., V. 48.
137. Heller and Weiss: Ztschrft. f. d. ges. exp. Med., V. 2.
138. Holzknecht and Olbert: Ztschrft. f. klin. med., V. 71, p. 91.
139. Hofmann, F.: "De Morbis oesophagi spasmodicis opera omnia," Edit. Geneva, p. 130. Cited by Zenker and Ziemssen.
140. Sauerbruch, Bruns Beitrage, V. 46, p. 423.
141. Beck: Naturhist. med. Verein. Heidelberg, 1917.
142. v. Ziemssen's Handbuch, V. 7, 1st. appendix.
143. Stark: "Die Divertikel der Speiserohre," Leipzig, 1900, p. 45.
144. Laimer, Monro: "The morbid anatomy of the human gullet, etc.," Edinburgh, 1911, p. 12.
145. v. Bergmann: Munch. med. Wchschrft., 1890, p. 819 (Virchow's discussion).
146. Jacobs: Deutsch. med. Wchschrft., 1912, p. 997.

- 147. v. Hacker: Handbuch d. prakt. Chirurg., 4th ed., V. 2, p. 513.
- 148. Guiscz: Soc. des Chir., Paris, Nov. 18, 1910. 148. Kreuter: "Die angeborenen Verengerungen und Verschlüssungen des Darmkanals, etc." Leipzig, 1905.
- 149. Frankel: Virchow's Arch., 1902, 167, 92.
- 150. Kummell: Munch. med. Wchschrft., 1906, p. 453.
- 151. Kermauner: Wien. klin. Wchschrft., 1898, p. 974.
- 152. Heinlein: Munch. med. Wchschrft., 1911, p. 436.
- 152. Roy: Lancet, 1911, p. 1765.
- 153. Kappis: Mitt. a. d. Grenzgebiet, 1910, 21, 746.
- 154. Rost: Deutsch. med. Wchschrft., 1912, No. 36.
- 155. Cohn: Mitt. a. d. Grenzgebiet, 1908, 18, 295.
- 156. Brosch: Virchow's Arch., 1900, 162, 114.
- 157. v. Lichtenberg: Naturh. med. Verein., Heidelberg, 1907; also Munch. med. Wchschrft., 1907. Petren: Brun's Beitrage, 1909, 61, 265. (Lit. from Scandinavia.)
- 158. Girard: Chirurg. Kongres, 1913. Moutón: Brun's Beitrage, 1919, V. 115.



## CHAPTER II

### STOMACH

The advent and subsequent general use of the x-rays and fluoroscopy have made possible a far more thorough and precise study of the **form** and **movements** of the stomach than the older methods of investigation used in experiments on animals which necessarily perverted the physiology. Pathologically, a whole series of new disease pictures have been discovered, and new symptoms added to known diseases. Many of these local diseases are not only curable, but their treatment often brings about considerable improvement of the general body health.

From the surgical standpoint, greater emphasis must be laid on investigations of the *motor function* of the stomach, than on its secretory activities, although both are very closely related. In examinations of the former with bismuth meals, the objections have often been raised that they are unphysiological, and give artificial results (Stiller). But experiments of Best and Cohnheim (1) have shown that the objections are groundless, except in the instance when bismuth is given with meat in dogs with fistulæ. In this case, evacuation shows later than it really occurs, and is due, in all probability, to digestive liquefaction of the meat and a consequent quicker evacuation of the food than of the bismuth. This latter substance, itself, causes slight retention of food both in the stomach and the intestine, so that barium sulphate is to be preferred, since it is free from this objection. However this may be, it is necessary before proceeding further, to make certain that the form and movements of the stomach are not altered by bismuth but are shown in their true physiological relations. A number of procedures have been employed to demonstrate this very important point, and the instructive one of Grodel and Seyberth may be mentioned (2). They sewed silver beads to the greater and lesser curvatures of the stomachs of dogs, and took x-ray pictures with and without bismuth meals. In both cases the shape and movements of the stomach were identical.

When x-ray work was in its earliest stage, it was not very certain to anatomists that the stomach had a "*fish hook*" shape (Rieder), or the shape of a *cow's horn* (Holzknecht), as shown in the roentgenograms, but they soon satisfied themselves of the truth of the pictures. Among other methods, the organs of executed criminals were fixed very quickly after death by the intravenous injection of formalin, and then it was discovered



that the shape of the stomach was the same as that shown by x-ray methods in the living (His, Simmonds, (3)). As a matter of fact, this procedure had been done some time earlier, and a few surgeons and anatomists had a fairly clear knowledge of the shape of this organ, but only with the increasing use of the x-rays has this knowledge become general (4). According to the newest investigations, the cow's horn shape of Holzkecht must be regarded as the physiological one. Even the siphon form is a sign of visceroptosis, although it is seen in so many individuals that, without further findings, it cannot be considered pathological, especially since the evacuation time in this type may be quite normal (5). Further important details of its shape may be summed up as follows: the empty stomach is a pouch with many folds, whose walls lie, ribbon like, in contact (6). The plaster model of His shows beautifully that the greater curvature is forward when the arcuate fibres contract, so that the anterior surface of the stomach faces superiorly. The pylorus then points backward, and is covered in part by the greater curvature (7).

Functionally, *three divisions* of the stomach must be recognized, the cardiac portion, the pyloric antrum, and the pylorus itself. [It is perhaps even more convenient and certainly better for purposes of thought to further subdivide the stomach, as done by Cannon. Accordingly, the cardiac portion is subdivided by a line drawn horizontally through the cardia. Above the line is the fundus, below and to the incisura angularis is the body. The pyloric portion is also divided into the pyloric vestibule and the pyloric canal (8).] The cardiac end is the largest part, and represents, so to speak, a store room; while the antrum is the motor portion for the transport of its contents (9). There is, of course, no sharp anatomical boundary between these two divisions, but in man, as well as in dogs (10), a deep annular indentation can be observed, which is constant in position and is formed by a pulling in of the greater and lesser curvatures. This represents, so to speak, a functional sphincter (11). These contractures at various places of the stomach have excited considerable interest of late, chiefly from the investigations of Aschoff (9). Anatomically, the "narrow passes" as he calls them, are formed from contractions of the musculature and from folds in the mucous membrane (12). The more detailed architecture of the musculature and its relation to the shape are discussed by Forssell (13).

Interesting details of the nature of *gastric peristalsis* have been given, especially by Schwartz (14). It seems that the form of a contraction wave depends on the thickness of the musculature. In a stomach with thick walls the contraction wave is short and deep; conversely, in a stomach with thin walls it is long and shallow. But according to the studies of A. Muller (15), the number of layers of a stomach varies; separate muscle

bundles may lie above or below each other, depending on the state of tonus of the wall at the particular time. In general, the muscle increases in strength towards the pylorus. The contraction waves therefore become deeper as they approach this part. Since the lumen decreases at the same time, the opposite walls of the antrum finally touch during a strong contraction and there results a trapping of the food mass by the action of the so-called "sphincter antri." Such trapping occurs in other parts of the stomach under pathological conditions (12). We assume from the mode of formation of this "sphincter" that it does not always appear at the identical anatomic place, but always approximately there, and that, as Kastle, Rieder, and Rosenthal emphasize (16), it constantly relaxes and reforms as peristaltic waves progress from the fundus along the greater and lesser curvatures.

The fasting stomach is a lumenless, closed pouch, and when food enters, it expands, not so much by the weight of the food, as by the action of a nervous mechanism in the stomach itself. The recognition of this active unfolding is of great importance in understanding many physiological and pathological conditions. Why, for instance, does food which does not tempt the palate like some favorite dish, satisfy so quickly? Fleiner's (12) (p. 113) explanation is that complete unfolding does not take place; he calls it quite apropos, "defense reflex," and quotes a number of correlated examples occurring in various gastric diseases (17). The expansion of the stomach is also dependent on the consistency of the food, for in the case of solids, it remains in the highest part of the fundus for some minutes, and then, slowly and wedge-like, pushes downward, gradually overcoming the tonus of the musculature (18). Several minutes are necessary after the last bolus has been swallowed for the chyme to reach the most dependent part. Fluids, however, flow downward very quickly, like a rivulet, and only expand the stomach laterally when they have reached the lowest level. They are said to flow along a gutter on the lesser curvature when the stomach is filled with solid food (sulcus gastricus) and to quickly reach the pylorus without diluting the contents at all (19). The fact that the erosions are usually found along the lesser curvature in cases in which caustics are swallowed after a heavy meal, is supposedly dependent on this distribution. According to Kastle (20), however, this gutter cannot be demonstrated by the  $x$ -ray, and Schuller (21) questions its presence in man.

Generally speaking, the movements of the fundus and antrum are distinctly different. Those of the former are chiefly of the nature of tonic contractions; kneading and mixing does not take place here but the food simply accumulates in layers as it is swallowed and the masses which enter last, lodge in the center of the food bulk (22). Liquefaction

proceeds at the surfaces and as the food is digested it is forced toward the pylorus by peristaltic waves which show roentgenologically, as shallow segmentations of the curvatures (23). Finally, the food is pressed into the actual motor segment, the antrum. Here, the movements are very powerful and consist of rhythmic contractions and relaxations. As demonstrated in the studies of Duccesi (24) there is an actual "systole and diastole." They are therefore mixing and propulsive, and succeed each other with amazing regularity. Cannon (23) who introduced the *x*-ray method in the study of digestion, states that in cats, they occur at the rate of six per minute, and can be observed in action with machine like regularity for over seven hours. In man, according to Holzknecht, the contractions occur about every 22 seconds. Kastle (20), (11), however, with his co-workers, has made kinematographic studies of these movements and states that such a division of the stomach into antrum and fundus is not possible as far as the gastric movements are concerned.

The *stimuli* which excite gastric motility are first, mechanical; and second, chemical. The empty stomach is usually quiescent, but every hour and a half to two hours and a half, there is activity of the entire gastrointestinal tract, lasting about 10 minutes, and directed towards moving the contents forward. This was first observed by Pawlow and Boldireff (25), who also found that the digestive glands secrete during this period. Very slight mechanical stimulation is sufficient to initiate movements (24) even touching with a bougie, but the temperature of the food seems to have little influence, particularly on the rate of evacuation (Egau (26)). Of chemical stimulants, hydrochloric acid and pepsin, both physiological products of gastric glands, are by far the most active.

[But the increasing amounts of digestive products, probably after absorption, are also a potent stimulus. As Duccesi points out, gastric movements are initiated by the entrance of food, further stimulus is provided by the secretions, particularly the acid, and the final one by the digestive products themselves.]

It is interesting to observe that hydrochloric acid seems to act antagonistically in the fundus and antrum; it increases the peristalsis of the former and diminishes that of the latter, and in high concentration, may not only completely inhibit the movements of the antrum, but actually incite anti-peristaltic waves (Duccesi (24)).

[In other words, the excitability of the neuromuscular apparatus varies not only quantitatively but also qualitatively in the several parts and is almost antagonistic in the region of the antrum as compared to other parts of the stomach (Duccesi).]

The third functionally distinct part is the *pylorus*. It is open in the fasting stomach and *x*-ray studies have shown that when food first

enters, it can be pushed through into the duodenum by pressure applied to the abdominal walls (5). The movements of the pylorus, which in opening and closing are directed toward the bowel, are regulated minutely by reflexes arising in the mucosa of the stomach and duodenum (27), (19). If, for example, in a dog with a duodenal fistula, the ileum is empty, the antrum during each contraction projects a stream of chyme, at first well digested, later imperfectly so, through the fistula (28). But if the material escaping is now injected into the duodenum, distal to the opening, the pylorus closes, and remains contracted until the acidity of the injected material is neutralized by the alkaline intestinal secretions (Tobler). Thus the pylorus closes when acid is brought into contact with the duodenal mucosa, and the same phenomenon occurs with fat. It also closes when solutions of a strength other than isotonic are introduced into the stomach (29); when the temperature of ingested substances differs considerably from that of the stomach (30), and when painful stimuli of all sorts are present (9).

[The acid control of the pylorus has undoubtedly been overemphasized. Cannon, who elaborated this theory, early recognized its inadequacy in the explanation of many of the facts observed in the emptying of the stomach, notably in the emptying of fluids. Recent experimental work on man and animals, using various methods, have correlated the opening and closure of the pylorus with the movements of the stomach itself. Thus under normal conditions the human pylorus opens regularly at the end or height of each tonus contraction. To use the expression of Cole, during the systole of each gastric cycle the pylorus opens and allows a small stream to be forced through. During diastole the pylorus may be closed, and Cole believes, this prevents the chyme from dropping back into the stomach as the intragastric pressure diminishes. Furthermore, since it is the so-called "duodenal cap" which is filled when the stomach contents leave the pylorus, particular interest, especially from roentgenographic studies, is attached to this portion of the duodenum. Numerous considerations lead to the conclusion that it should be classed with the stomach and not the intestines. It seems that further work is necessary to determine the factors which influence the emptying of this cap. Probably the state of fullness of the small intestine is a very important factor, but the reaction, or the fluidity of the contents of the cap may also play their parts. These questions are of extreme importance in a consideration of duodenal ulcers, the great majority of which occur in the first portion of that organ. Luckhardt, Phillip and Carlson (31), for example, found in their experiments that the intragastric contents as they issued from a duodenal fistula were acid to phenolphthalein, although they rarely showed free acid to other indicators (32)].



The **secretory** function of the stomach is of somewhat less interest to the surgeon than the motor, and even though the former has been much more extensively studied, it is not the better understood division of gastric physiology (33). The *gastric juice* is supplied chiefly by the fundus, where the long tubular glands are crowded closely together and consist, as we know from Heidenhain's time, of the chief and the parietal cells. The former are said to secrete pepsin, the latter, hydrochloric acid, but this has, as yet, not been proved beyond doubt. The gastric juice furthermore contains a lipase (34), a lab ferment, many inorganic salts, a nucleoprotein, whose import is not clear, and mucus.

The function of these glands has been studied successfully only since Pawlow (35) devised methods in his classic experiments, for constructing miniature stomachs and for utilizing stomach and duodenal fistulæ (Tobler (27), Cohnheim (9), and others). We know now that the secretion of gastric juice is essentially a reflex process and may be initiated not only from the mouth by chewing and swallowing, but even the desire to eat, leads to secretion. It can probably also be regulated from the duodenum, for Cohnheim and Marchand (36) found that the introduction of hydrochloric acid into that organ was followed by a diminution of hydrochloric acid production in the stomach. Conversely, soaps in the duodenum arising from fats, lead to an increased secretion of acid. This latter fact has a certain significance, as we shall see later, in the secretion of gastric juice after cholecystectomy. Thirdly, the activities of the glands of the fundus are stimulated from the antrum, it is said, by means of a hormone (37) which is formed when digestive products are absorbed from the mucosa of that part of the stomach. That this is probable may be concluded from the observation, among others, that after atropin is given, the nervously controlled gastric secretion is inhibited, but abundant secretion can be elicited from stimuli arising from the antrum (38). Nor should the importance of the intragastric ganglia to secretion be underestimated, for the stomach will continue to secrete, even when all the extrinsic nerves have been severed (39). In this case it is possible that certain chemical substances, after absorption, are carried to the intrinsic nervous mechanism and thus activate the glands without the cooperation of the extrinsic nerves (see Babkin (33)).

The gastric glands secrete a juice which is often qualitatively and quantitatively quite different under the influence of these different stimuli. This extraordinary sensitiveness can be seen from Pawlow's investigations, in which the juice secreted varied considerably with the type of food ingested. Thus with bread, meat, milk, etc. an entirely different composition was found. Warming the food has a decided effect, so that temperature is also a further factor. Since much of our knowledge

of these processes has been gained from animals, great importance is attached to the studies on man, which show that the animal results in general can be applied directly to human physiology (40).

The gastric juice, like other digestive fluids, when first secreted contains its enzymes in a form inactive for digestion. The name given to these pre-enzymes is zymogen, and there are usually special substances which are best adapted to activate them. In the case of pepsin, it is the hydrochloric acid. This enzyme is the principal one of the gastric juice and therefore in the stomach it is the protein of the food which is attacked, since the activity of pepsin is applied to these substances. Cleavage is carried to albumoses or proteoses (41).

Carbohydrates are not attacked, but on the contrary, the ptyalin of the saliva is destroyed. Since, however, the food masses are deposited in the center of the stomach and do not at first come in contact with gastric juice (22), carbohydrate digestion may progress from admixed saliva for some time. An actual digestion of fat does not occur in the stomach, it is only liquefied there. Rennin has great physiological importance during the suckling period. It coagulates milk by precipitation of the casein and renders it more freely digestible. [The question of the identity of rennin and pepsin is often in controversy. There seem to be more facts in favor of their separate identities, but more investigation is needed to decide the matter conclusively. There are also assertions that fat may be digested in the stomach. These need corroboration.]

The question of **absorption** from the stomach, particularly of proteins, has been generally answered in the affirmative, mainly from Tobler's (27) investigations. Recently, however, a paper has appeared by Tsche-kunow (41) which is worthy of exceptional notice. According to his work, no absorption whatever of proteins takes place in the stomach, and Tobler's findings must be considered due to experimental errors. Tsche-kunow's work was done so carefully, that we must conclude not only that absorption does not take place but is actually improbable.

The ability of the stomach to absorb water is a particularly important question for surgeons. Under ordinary conditions, the amount absorbed is negligible. The process begins first in the ileum, therefore, in pyloric stenosis, the patients often become desiccated. [Other substances such as glucose and alcohol are absorbed with a fair degree of facility, and probably also hydrolyzed protein. These absorbed products go to make gastrin, the hormone which stimulates secretion after the psychic flow ceases.]

The normal physiology of the gastro-intestinal tract of the *suckling infant* may be found discussed by Uffenheimer (42).

These complicated motor and chemical activities of the stomach are regulated by a marvelously delicate **nervous mechanism**. The funda-



mentals of the innervation of the entire gastrointestinal tract are similar, so that the general principles may be first discussed, and then the differences in various parts elaborated. Our knowledge of the innervation was gained chiefly through the work of Langley (43) and his school. Additional work was contributed by Openchowsky (44), Magnus (45), Pawlow (46), Bayliss and Starling (47), Elliot and Smith (48), Popielski (49), Goltz (50), v. Frankel Hochwart and Frohlich (51), Courtade and Guyon (52) and many others.

In the first place all organs containing smooth muscle fibres, possess ganglia lying in the muscle substance. These are known as the plexus of Auerbach and by means of this nervous apparatus, the intestine is able to execute rhythmic movements and propel any contents forward even when removed from the animal body.

The second nervous apparatus in the intestinal wall is the plexus of Meissner which controls the movements of the muscularis mucosæ (Exner (53)). This thin band of muscle protects the mucosa from injury by pulling it away from sharp or jagged objects, or rather by a lowering of tone, it allows the mucosa to belly away.

Two groups of nerves, which in general, have opposing actions enter Auerbach's plexus. The first are *sympathetic fibres*, and the second are fibres from the *cranio-sacral system*, i.e., from the brain and spinal cord. Broadly, the antagonism of these two groups is such that when stimulation of the one produces contraction of the muscle, stimulation of the other produces relaxation, although in a given case, it cannot be predicted which of these two effects will be produced. It must always be remembered that a stimulus flowing through a nerve does not go directly to the muscle, but to Auerbach's plexus, in which it may be further elaborated. And then again, the separate segments vary in the degree of influence exerted on them by central innervation. The ileum is the most independent, while the stomach is very considerably under the control of the extrinsic nerves, even though it does, like the ileum, carry on rhythmic movements outside the body. V. Openchowski (44) assumes in the case of this organ that the independent activity occurs by reason of special groups of ganglion cells located under the serosa and demonstrated by him with the gold chloride method. These cell groups are said further to correspond broadly to Remak's cells in the heart.

The *impulses from extrinsic sources*, transmitted to the stomach through the vagus and sympathetic may be divided into motor, sensory and secretory, and the motor function, especially of the vagus, has been investigated very extensively (54).

Summing up, this nerve carries both stimulating and inhibitory fibres to the stomach, so that stimulation of the peripheral stump causes first

inhibition (55), then increase of gastric motility, while bilateral section in the neck causes slowing of the movements (Cannon (56)). Those of the antrum in particular, are made more active by vagus stimulation (Braun-Honckgeest (57)).

A *communication exists between the right and left vagi* on the anterior surface of the esophagus (Ducceschi (58)), so that on section of one in the neck, no motor disturbance of the stomach is demonstrable. On the other hand, since communications do not exist in the stomach itself that half of the stomach whose vagus has been cut is not affected by stimulation of the other nerve. On section of both vagi the gastric movements become slower and more superficial (Cannon (56)). We may assume there are separate tracts, corresponding to the different functional divisions of the stomach. In like manner, there are separate centers in the brain to which these tracts belong, although they must be in close communication (see Openchowski (44)).

The *splanchnic nerves*, as antagonists, carry chiefly inhibitory fibres to the stomach and stimulation of the sympathetic at the upper level of the dorsal spinal cord leads to inhibition of peristalsis (see Openchowski (44)). Section leads to no demonstrable change in gastric movements, so that even when all four are cut, the difference in the evacuation time of carbohydrates and proteins persists (Cannon (56)). The cross relation of the vagus and the sympathetic, which will be discussed under "Vomiting," is shown in the experiments of Klee (59). The results following nerve separations will be discussed later.

The *center of inhibition* of both large and small intestines is the cœliac plexus (Popielski (49)). Its destruction leads to pronounced increase in motor activity as a clinical case (tumor metastasis) and the investigations of Exner and Jaeger (60) show. Ileus may even be suggested by the intense spasms of the ileum and colon.

How far this increased intestinal motility can be brought into relation with the *vaso-motor functions of the sympathetic*, i.e., with constrictions and dilatations of the vessels, is unknown at the present time. The motor activities of the stomach, on the other hand, are not influenced to any noteworthy degree by either section of the sympathetics (Cannon (56)) or by extirpation of the cœliac ganglion (Aldehoff and v. Mering (28)). Secretion of gastric juice also takes place in a stomach devoid of nerves (Popielski (38)).

[At this point, the theory of intestinal movements as propounded by Alvarez may be introduced. According to most text-books, food material is said to move aborally because of the myenteric reflex or Bayliss and Starling's "law of the intestines" which declares that stimulation at any point produces contraction above and relaxation below. This is inade-

quate to explain many of the normal phenomena and is of less help in pathological conditions. It had been observed by a number of writers that the small bowel varies in its muscular strength and tone, and in its rhythm and irritability in different segments. In a series of papers, Alvarez and his co-workers have brought out the fact that there is a gradient in these properties from the stomach and including that organ, downward. Strength, tone, rhythm and irritability, all diminish as the terminal ileum is approached. When food is introduced into the stomach, its tone, using the word in a loose sense, rises and the contents are moved into a less active and less sensitive region. The tone of this portion then increases, and the contents are again moved forward and so on. Reverse peristalsis would occur if, for any reason, a lower segment should become hyperactive or if the tone of a higher segment should become less. Since ordinarily the higher segments are the more sensitive and active this would hardly occur except for short stretches or in disease. Furthermore, the intestines in spite of their length, act very much as a unit, so that each segment knows so to speak, what the other is doing, probably by way of short nerve paths through Auerbach's plexus and through the mesentery and ganglia. One part of the tract responds almost instantly to changes in another. Reference to this subject will be made again. In discussing the emptying of the duodenal cap (p. 40), it was said that the state of fullness of the intestines was an important factor. Applying the theory of gradient, the tone below may be increased on account of the presence of food to a point where it is equal to that in the duodenal cap. The gradient of forces then becomes a horizontal line and no progress is made no matter how great the other activity throughout the tube (61).]

Of the **pathological changes in gastric motility**, only that of *vomiting* will be mentioned here. With Openchowski (44) we may picture great restlessness in the viscera followed by spastic closure of the pylorus. Meanwhile saliva mixed with air accumulates and distends the lower end of the esophagus. A forced inspiration is made with the glottis closed, so that more air is sucked in. The cardiac orifice relaxes, and with it the cardiac end of the stomach, while strong contractions occur in the entire pyloric end. The organ assumes a pear shape and partly by its own movements and partly by the compression of the abdominal muscles, the contents are ejected upward.

In the final analysis vomiting is a result of stimuli reaching the center in the medulla, but they may be either direct or indirect. Certain chemical substances act directly (apomorphin, also morphin); other stimuli may arise in almost any part of the body, but particularly from the pharynx and throat, from the gastric mucosa, or the peritoneum. [The duodenal mucosa is a particularly favorable place from which to elicit vomiting

(31).] We will return to a discussion of the peritoneum in this connection later.

*Two paths for the innervation* of vomiting are described by Openchowski, depending on the type of emetic used; the one through the vagi, the other by way of the splanchnics, the branches of the sympathetic to the spinal cord, and from there to the quadrigemini. Klee (59) could show in decerebrated cats that stimulation of the vagus consistently produced vomiting, and the sequence of events in this case was first, closure of the pylorus, then diminution of peristalsis, contraction of the pre-pyloric part of the stomach, and finally opening of the cardiac orifice. The closure of the pylorus is a very important part of the act and since it is dependent on the splanchnics, vomiting was prevented when Klee sectioned these nerves.

On the basis of the considerations mentioned above, a number of remedies have been proposed for the vomiting during and after anesthesia (v. Brun (62)). Washing of the stomach with sodium bicarbonate has been used (Lenewitsch, Gunby); giving vinegar by which the chlorin derived from chloroform may be combined; finally, compression of the vagus and phrenic nerves lateral to the jugular vein (Joos) are all procedures, among many others which have been recommended. Individual differences and sensitiveness play such an important role in this type of vomiting, however, that any results from treatment must be judged with the greatest caution. [A particularly pernicious vomiting after anesthesia occurs in individuals whose renal function is impaired. We have often observed it following prostatectomy. The administration of sodium bicarbonate as suggested above, has certain experimental and clinical justification. In these renal cases, there are a number of factors operating in a vicious circle. There is not only retention of metabolic products, but a perversion of metabolism which gives rise to the well known ketone bodies and probably other as yet unidentified partial oxidation products. This determines a tendency to acidosis, which in its turn leads to the formation of additional acids, and so on. Fluids freely given, are of great benefit, but the question of whether the addition of an alkali assists is difficult of solution. This subject will be discussed in more detail in the following pages.]

The **sensory tracts** of the stomach lie both in the *vagi* and *splanchnics*. In the former, the communication between the two nerves on the anterior surface of the esophagus is doubtless as important in sensory phenomena as in motor. The sympathetic fibres enter first the coeliac ganglion; from here they travel via the major splanchnic, through the rami communicantes to the posterior roots of the spinal cord (7th to 9th according to Head, see Foster and Kuttner (63)). Thus when sensory stimuli reach the



vagus centers from the gastric mucosa, they give rise reflexly to motor and secretory responses which are then transmitted to the stomach. This entire arc is of course below the centers of consciousness; at least, in operations under local anesthesia, patients feel nothing when the gastric mucosa is cut and sewed. We will speak of the sensory phenomena in more detail in discussing the sensitivity of the abdominal cavity as a whole.

The question of the origin of the *pain in gastric ulcers* has been much discussed. Lennander (64) is of the opinion that its perception comes through the parietal peritoneum and it may even arise from the absorption of an abnormal lymph, *e.g.*, one with a high hydrochloric acid content. Muller (65), Talma (66), and others believe that the hydrochloric acid, *per se*, excites the pain. But that this opinion is not correct, has been shown by J. H. Schmidt (67) and others who poured hydrochloric acid into the empty stomach of patients with gastric fistulæ and no pain was elicited.

On the other hand, all sorts of psychic emotions like joy and pain, produce both increase and decrease of the activities of the stomach. Cannon's observations with the x-ray on the slowing of antrum movements when his cats were teased, Pawlow's obtaining the same results by sensory stimuli from the periphery, give us fundamental facts in the application of diets for our patients.

[Psychic states play such an important role in all the functions of the stomach that great care is necessary in the interpretation of any studies of its secretory and motor activities. Not only does tasting or chewing food produce an abundant flow of gastric juice, but even the sight or smell of it stimulates secretion of what has been called the "appetite juice." But a distinction must be made between appetite and hunger. The former is highly complex involving the highest centers whereas the latter has a much simpler basis. Particularly through the work of Carlson and his associates, it has been shown that hunger is related to contractions of the stomach. His studies have been made on lower animals, on a man with a gastric fistula made because of esophageal stenosis, and on normal men. By the use of balloons in the stomach connected to suitable manometers and recording devices and by the use of two balloons, one inside the other and separated by a layer of bismuth paste, so that x-ray observations could be made, he has described two main forms of contraction in the empty stomach. The first is a "tonus rhythm," caused by tonic contractions of the fundus, and the second is of the nature of powerful rhythmic contractions which are superimposed on the tonus rhythm. These may increase in amplitude and frequency until a tetanus results which after persisting for a short time subsides and is succeeded by a period of rest after which the same cycle is repeated. It is during the periods of



contraction that the sensation of hunger is experienced, and the sensation varies directly with their strength until, during tetanus, veritable pangs may be felt.

The origin of these contractions has been carefully studied and it seems that so far as they are dependent on tonus and motor stimuli through the vagi, the impulses do not originate in the cerebral hemispheres. Complete section of the splanchnics leads to increase of tonus and augmentation of the contractions, while section of the vagi in the chest gives rise to hypotonus and disturbance in the rate and regularity of the rhythm. Much data indicates that the neuro-muscular apparatus of the empty stomach is somewhat unique in its freedom from control by afferent impulses and central processes. The contractions are not only present during sleep when practically all other similar mechanisms exhibit lowered tone, but may even be augmented. Since it is the contractions which are reflected into the consciousness as hunger, the actual sensations may be deadened or abolished by concentration on other subjects, as for example, doing a sum, or reading. But the contractions continue whether they are perceived or not. The idea has been expressed that the ordinary routine of eating three meals a day is largely a habit which can be changed at will. A man may accustom himself to two meals a day and experience no hunger. Careful research has shown that while such individuals may not experience hunger, there occur nevertheless, gastric contractions as soon as the stomach is empty or practically empty, and the sensation is not perceived because of strict attention to other matters.

These questions are of intense practical as well as theoretical interest. Many a case of hunger contraction has probably been called hyperperistalsis. To return to the question of the pain in gastric ulcers, it is not an unusual history which says that the patient places a glass of milk and some crackers or other food beside his bed so that he may allay the pain which often wakes him at night. In fact, it has been remarked, facetiously perhaps, but there is truth in it, that with such a history, the diagnosis can be made over the telephone. We know hunger contractions occur during sleep and it is most interesting that a study by Carlson (68) should show contractions during the pain in one of his subjects. This line of investigation may prove of occasional diagnostic importance in diseases of the upper abdomen, although if the ulcer pains result from contractions, either from hunger or digestion, similar pains may be produced also by other pathological conditions which excite hypermotility or normal motility with hyperexcitable nerves, a thought which agrees perfectly with clinical experience.

It is not surprising if the pain is due to contractions, that the acidity does not parallel the intensity of the pain. Movements of the stomach

are independent, to a certain degree, of the reaction of the contents, but the pylorus is more sensitive, and hyperacidity may augment its contractions as well as those of the duodenum. In this case especially, the administration of alkali would temporarily ease the pains. That many ulcers should be accompanied by very little or no pain is also clear. There are variables in the forms of gastric, duodenal and pyloric contractions, inflammation and edema, proximity to nerve endings, *viz.*, the vagi, and the inherent nervous stability of the individual. It also follows directly that the cessation of pain is no criterion of healing of the ulcer (69).]

The vagus also carries *secretory fibres* to the stomach, for as Pawlow found, electrical stimulation causes an outpouring of gastric juice. Section leads to abolition of the reflex flow, *i.e.*, of the appetite juice during feeding (46). But the statements regarding the influence of innervation on the secretion of gastric juice are by no means beyond criticism (see Babkin (33), Rheinboldt (70)). It is said that high section of both vagi brings about an increased production of hydrochloric acid, which leads to spastic contraction of the pylorus and subsequent gastrectasia (Katschkowsky, Fritsch (71)). The formation of pepsin is also diminished and fermentation of the stagnating food is likely to occur.

Aldehoff and v. Mering found diminution of acidity at first after section of both vagi below the diaphragm, but this effect disappeared in about fourteen days. Nothing is known of the influence of the sympathetic on this process.

The extrinsic nerve supply of the stomach has recently become of quite especial interest to the surgeon, because modern operations on the thorax, especially on the esophagus, often come in conflict with the vagi, and secondly, section of these nerves has been advised in the gastric crises of tabes. At times good results have followed this operation (Forstner and Exner).

*Gastric crises* are a complex of sensory, motor and secretory stimuli in the region of the stomach. Forstner and Kuttner assume that the sensory phenomena are primary, and reflexly these excite motor and secretory changes whereby vomiting and gastric secretion occur. Reasoning in this manner, Forster and Kuttner (63) severed the sympathetic fibres, which as stated, lie in the seventh to ninth dorsal segments, and they as well as other operators, obtained good results in a large number of cases. Not all were benefited, however; vomiting, especially, was often entirely uninfluenced, so that Exner (72) was led to sever the second tract which controls vomiting—that running in the vagus—by cutting that nerve at the cardia. His results were also good. From the pathological physiological standpoint, it must be admitted that both methods are based on good logic. Disease of the vagus nuclei in tabes has often been described and

Exner could actually demonstrate inflammatory changes in the peripheral vagus in a number of his operative cases.

On the other hand, vomiting may also be incited through the sympathetics, and that operative method which not only removes one symptom, but like Forster's, improves all of them more or less, deserves the preference. Most surgeons therefore destroy the sensory part of the reflex arc, and thus all of the symptoms, especially the pain are improved. If vomiting is not terminated by this, the advisability of section of the vagus must be considered. The effects on the stomach of this latter operation are less in subdiaphragmatic vagotomy than after higher section. Aldehoff and v. Mering sectioned the vagi, then cut transversely across the esophagus just above the cardia and reunited it. They found no changes in the motility or secretion of the stomach and especially no secondary dilatation following this operation except during a short time in which a delay in the evacuation and a reduction in hydrochloric acid secretion were observed. After section in the neck, below the point where the fibres to the heart separate, there are slowing of the movements, increased hydrochloric acid production, pylorospasm, and gastrectasis (Cannon, Katschkowsky, Fritsch).

With good care, animals remain alive after high vagus resection, but their digestive tracts are extremely sensitive (Krehl (73)). The difference in the behavior of the stomach after this operation and subdiaphragmatic vagotomy, seems to lie in the fact that sympathetic fibres are also cut in the latter procedure and according to Cannon (56) gastric movements are practically undisturbed when both vagi and splanchnics are cut. Whether similar conditions hold true for secretory processes, is as yet, unknown, although it seems not improbable. Complete section of all sympathetic and vagus fibres is done when a so-called circular resection is performed. We shall return to the subject of gastric movements after resection in discussing operative methods.

Gastric movements are altered when the pylorus is closed too tightly. The ability of the remaining part of the stomach to move remains normal, but it must labor against an abnormal resistance. The first type for consideration is that occurring in infants, which according to numerous investigators, is probably a spastic contraction of an hypertrophied pyloric muscle (74). Such cases of **pylorospasm** are also occasionally met in adults, although the contractures are not so severe and lasting. Wilms (75), especially, has called attention to this condition, and has advocated x-ray therapy. Manasse (76) has described cases of pylorospasm, in which varices and similar conditions existed in the stomach wall. These pylorospasms should probably be considered secondary. They occur quite frequently with ulcers, and much clinical evidence has shown that

the ulcer need not be at the pylorus, but may be distant. In fact, other conditions in the stomach, as well as in the intestines, with or without mechanical obstruction to the pylorus, may lead to six hour retention with secondary pylorospasm as its cause. Holzkecht and Luger (17) have described secondary spasms in other regions of the stomach.

[From what has been said of gastric movements, regarding the theory of gradients, and from other considerations, it is clear why pylorospasm should result from diseases of other viscera, *e.g.*, the gall bladder.]

There are, furthermore, symptom complexes, in which, with a normally functioning pylorus, there is **defective evacuation of food** which must be attributed to a paralysis of the body of the stomach. Even in a stomach previously healthy, a sudden motor insufficiency from the action of certain injurious factors may occur. Immense quantities of gastric juice, bowel contents, and consumed fluid, collect, to be vomited periodically. Since water is not absorbed by the stomach, desiccation of the patient takes place and finally death ensues.

In *acute dilatation*, a condition of the utmost interest to surgeons, it is necessary to sharply differentiate between two forms of the disease, that due to a mechanical obstruction, the so-called *arteriomesenteric ileus* and the *true paralytic form*. Either may undoubtedly exist alone, but they often exist in combination; the former may be the cause of the latter, and thus the symptoms may be much confused. In the first place (Braun, Tuffiers, Payers (77)) there is an individual predisposition to this dilatation but its exact nature is not clear since the histories of the patients, as reported in the literature, give data concerning the gastric motility as it was affected during the attack, and not as it was before. The most probable explanation is that there existed a chronic insufficiency and an acute attack was superimposed, but there are a number of injurious substances which may produce sudden dilatation of the normal stomach.

Anesthesia should be mentioned first and accurate investigations on anesthetized humans have been carried out by A. Payer. In anesthetized animals the stomach may be enormously distended without rupture while in conscious animals this is not possible. Authors agree that anesthetics paralyze the stomach but their further opinions are conflicting.

Kelling (78) believes the paralysis is confined to the "evacuation reflex" and assumes there is a special valve mechanism in the cardia, whose opening is prevented by the anesthetic. Braun and Seidel (79) believe from observing the stomach "lying motionless under the abdominal walls" that there is a paralysis of the gastric center, and that the valve observed by Kelling is a secondary result of the distention. Payer's criticism of Kelling's valve theory is quite just. Such patients vomit



really enormous quantities and this fact contradicts any mechanical closure at the cardia.

According to Kuru (80) the primary factor in acute post-operative gastric dilatation is an insufficiency of the adrenals.

If we assume, then, that in this condition there is a motor paralysis of the stomach as a whole, the question arises, on which part of the nervous apparatus does the anesthetic produce its effect? That vagotomy leads to gastric dilatation and delayed evacuation has already been mentioned. Apparently the vagus can have no relation, however, to post-anesthetic gastric dilatation, because after section of the nerves as in Mangold's experiments (81) the same disturbances of innervation were observed. At least this occurred in birds. In Braun and Seidel's experiments, the splanchnics, sympathetics, and spinal cord were all sectioned and still the same phenomena were noted. Therefore, Payer's view that Auerbach's or Openchowsky's plexus is damaged is much more acceptable. According to him, it would otherwise be inexplicable "why motor insufficiency of the stomach lasts so much longer than the other effects of the anesthetic."

But it must be remembered that such gastric dilatation may occur without general anesthesia and may be found after operations under local anesthesia, or even without operation; for example, after applying a constricting bandage, such as a plaster corset (Kelling); during or after a debilitating disease such as typhoid fever; or in chronic suppurations (Kuru (80)); after catheterization of the bladder (Braun (77)); or of the ureters (Leguen (77)); after a fall (Tuffir (77)); after excessive eating (Korte (82)); and so on. While the blame in certain operations, *e.g.*, cholecystectomy, is laid on a local peritonitis or perhaps the gauze tamponade, in other cases the reflex factors must be considered, which are possibly similar to those producing the dilatation of the bladder so often seen after all sorts of operative procedures (Bier (83)).

A case of Haberer (84) was very characteristic in this respect, he observed a gastric dilatation presumably of reflex origin following the packing of gauze against the parietal peritoneum. The same influence is also shown in the investigations of Cannon and Murphy (85) who by merely manipulating the stomach and intestines, could demonstrate considerable delay in the evacuation of the stomach. In short, a large number of surgical procedures have been reported after which gastric dilatation occurred, and every experienced surgeon has seen cases in which this condition interfered with the operative success.

Gastric dilatation may kink and obstruct the third part of the duodenum by strapping down the root of the mesentery and its superior mesenteric artery. But this condition which is called *arteriomesenteric ileus* may take place without gastric dilatation (see Haberer (84)).



A large number of factors may cause displacement of the root of the mesentery, among them, lordosis, enteroptosis, abdominal drainage, post-operative displacement of abdominal contents, adhesions of loops of ileum in Douglas' cul de sac, from localized peritonitis (author's autopsy observation), emaciation, and so on. It is very often impossible to differentiate in a given case. The experiments performed by P. A. Albrecht (86) and repeated by P. Muller (87) serve rather to demonstrate the effect of the pull on the mesentery exerted by the ileum hanging down in the pelvis, than to clear up the etiology of arteriomesenteric ileus. They allowed the mesentery in a cadaver to hang with the pull directed toward the pelvis, and found the duodenum so completely kinked that water would pass into the jejunum only under very high pressure.

In addition to this acute type, there is also a chronic variety in which food remains in the stomach for an abnormal length of time and leads thereby to considerable nutritional disturbances (Mathieu and Roux (88)). In this condition also, the pylorus is patulous at first, but it is often combined with ptosis of the stomach (gastroptosis of Glenard (89)). There is a recent disposition to regard this *chronic motor insufficiency* of the stomach as a local symptom of a constitutional disease, an "asthenia" in Stiller's sense (90) (see Bauer (90)). Histological changes in the smooth muscle consisting of cloudy swelling and fatty degeneration have been described as an anatomical basis (Kussmaul (91)) but these are perhaps a result rather than a cause of the insufficiency, which finally depends on disturbance of innervation. Just what and where this disturbance is, whether it is along the vagus tract, or what seems more reasonable by analogy with acute dilatation, in Auerbach's plexus, is still entirely unknown.

In the first stage, it is the fundus which is particularly affected. As stated above, in the normal stomach, the longitudinally folded pouch is filled with fluid through almost its whole length before it begins to expand laterally; in atonic stomachs the walls are relaxed and lateral expansion takes place as soon as fluid enters, nor do they close tightly around the contents. Clinically, this is manifested by splashing noises when the stomach region is percussed. But emptying of the stomach contents may be nearly normal in this type, because, as was stated, the fundus only is affected, and not the pyloric portion which is the actual motor part. Retention occurs later, however, and if gastroptosis is present at the same time, it is assumed that the abnormal relations of the pyloric portion to the duodenum add another difficulty to evacuation. This is quite possible, and becomes even more probable if a small ulcer is found at the pylorus, as often happens in such cases. This type of ulcer is probably secondary to the nutritional disturbances in the sharply kinked portion.

(see Krempelhuber (92)). But another cause of incomplete evacuation is an increasing motor insufficiency. The stomach is then like a flabby bag which shows only weak defective movements under the x-ray. In such advanced cases, as Rovsing (93) has repeatedly emphasized, gastroenterostomy does not help, for the stomach lacks sufficient motor power to empty itself even through this opening.

[This opinion is now shared by practically all surgeons.]

The author can only support this much disputed opinion. He himself has lost a number of cases of gastroenterostomy done for marked retention, and at autopsy no other cause of the defective evacuation of the stomach could be found. The ultimate cause of the symptom complex is unknown. Reichmann (94) believed that a pathological hypersecretion of gastric juice was primary and overstretched the stomach. But Hayem's (95) anatomical investigations have shown that in almost every case of Reichmann's disease there is mechanical obstruction, either an ulcer or its scar. The hypersecretion should, therefore, be considered secondary, the result of a gastritis caused by stasis.

Before considering the changes in the motor and secretory functions of the stomach after various operative procedures, it is necessary to know something of the **histology of normal repair** in gastric and intestinal wounds (96). Small defects in the mucosa heal quickly and without any noteworthy disturbance. The lesion is narrowed by muscular contraction, and epithelium grows from the edges and covers it completely. The same principles apply to healing of the larger ulcers (Matthes (97)). The covering is derived partly from glands, and partly from the surface epithelium of the adjacent mucosa. Regeneration of glands occurs last, as a rule. Wounds of the musculature are reunited only by connective tissue. The healing of the serosa is the most important from the practical standpoint (Graser (98)) because fibrin is exuded over this coat at the slightest provocation and adherence to adjacent tissue takes place, but the endothelial cells are not necessarily destroyed by this exudation. If two serous surfaces are brought in contact and sutured, as is done so often in gastrointestinal operations, the fibrinous adhesions are organized; in a few days spindle cells and new blood vessels appear, and a firm union results. These fundamentals of repair are found after all gastro-intestinal operations. In most cases of gastroenterostomy (Marchand (96)), the mucosa of the bowel at the border toward the stomach is probably destroyed, even though the mucous surfaces are sutured most carefully. The repair of this area proceeds by granulation (Wilkie (99)) and the opening may narrow by cicatricial contraction (100).

The very nature of the conditions necessitates that gastric and intestinal sutures are early subjected to strain. The question arises, "How

much can they stand, without giving way?" Chlumsky (101) has tested on successive days following operation and under normal and pathological conditions, the strain to which various suture methods and buttons might be subjected without tearing. As controls, he used intact bowel and found that the healthy ileum of the dog supported a weight of 400 to 500 mm. Hg., while the ileum of man supports only about 200 mm. The greatest strength is shown by the submucosa, the weakest part in man is at the mesenteric attachment. In peritonitis, the bowel ruptures under much less weight. A double layer of sutures, just applied, will support a pressure of 150 and 200 mm. Hg. The Murphy button gives practically the same results. During the first four days, the firmness of the suture line becomes constantly less (as low as 20 mm. Hg.), then increases until about the eighth or tenth day, when it reaches a strength equal to that of the intact organ. Thus the greatest danger of rupture is from the third to fifth day.

If the figures for internal tension of the walls of the stomach during digestion, which, according to v. Kelling are from 8 to 10 cm. of water, are compared with these, it is seen that even under the most unfavorable conditions (third to fifth days) moderate amounts of fluids strain the line of suture only to one-third of its possible resistance. Kelling calculates even more favorably, and believes that with liquid diet the pressure rises only to about one-seventh of the danger point. At the same time, he cautions against solid food until the union of stomach and bowel is of connective tissue, since muscular contraction may increase the pressure considerably, and lead to rupture. Vomiting increases the internal pressure, but even in this case he believes that it will amount to only about one-fourth of the critical pressure.

The most frequent operative procedure on the stomach at the present time is **gastroenterostomy**, and in considering the changes in motor and secretory function following operations, this will be dealt with first (102). When the pylorus is present, but obstructed, the time factors of gastric emptying are very little changed and the belief that food leaves the stomach very quickly after gastroenterostomy is incorrect, as many careful studies have shown (103). When the stomach is empty, its walls are in contact and the gastroenterostomy opening is closed. Unfolding occurs only on the entrance of food, and filling proceeds normally. Its movements are in no way interfered with during respiration by the attached loop of bowel. When the last bolus of a meal was swallowed, that is, at the same time as in a normal stomach, Schuller could observe under the fluoroscope that some of the chyme separated and passed into the intestine. The contents do not leave in a continuous stream, but in single jets exactly as through the pylorus. When the gastroenterostomy opening is in the

antrum this similarity is more manifest because as Schuller could demonstrate in animals, the contents flow out in tune to the rhythm of the antrum movements. When it is in the fundus, the weight of the food is a more important factor and the stomach empties itself in irregular squirts (104). Herre (105) could also show a certain irregularity in the evacuation of the chyme. Since there is no ring shaped muscle at the operative gastroenteric anastomosis (106) it must be assumed with Kocher (107), and Schuller, that the periodic opening and closing is due to peristalsis of the loop of jejunum. Indeed, this was observed by Kocher during a laparotomy in a patient in whom a gastroenterostomy had been done previously. But perhaps a share in this emptying is assumed by the folds of the mucosa described above and by the contractions of the musculature in the so-called "narrow pass." At all events, the time of emptying of the stomach after gastroenterostomy is approximately normal; at least, it is not accelerated.

The clinical observations on this question are not in entire agreement, probably because they were made on pathological stomachs. We must therefore return to animal experiments, and especially to those done with the pylorus obstructed (Schoemaker (108)). If a gastroenterostomy is done either at the fundus or at the antrum, without coincident closure of the pylorus, the largest part of the chyme passes through the normal way and only occasional bits through the new opening (Kelling, Borszeky (109), Cannon and Blake (110), Legget and Maury (111), for opposite, see Kuttner (112). Schoemaker performed his experiments with the pylorus closed, and after gastroenterostomy or gastro-duodenostomy found by injecting acid into the intestine that the first squirt of chyme was evacuated into the bowel in about the same time as in the normal. He could obtain after either operation, a closure of the opening, which, however, was of shorter duration than the normal pyloric reflex. The evacuation of the stomach was especially quick after gastro-duodenostomy. Schoemaker points out, correctly enough, that these results obtained in animals cannot be applied in all respects to man. Nevertheless numerous clinical observations (Schuller (103), Barsony, and others (113)) some of which were undertaken to determine the usefulness of different methods of closure of the pylorus, have shown that gastric contents escape through a gastroenterostomy, provided it is large enough, in about the same time as in the normal stomach. Therefore the motor activity is little altered by this operation, but as we shall see, the *change in the chemistry* is quite considerable (114).

In the first place, there is a continual backflow of alkaline intestinal juice (115). Through this, and by alterations in the outflow conditions, gastric digestion is markedly influenced and proceeds quite differently. In



general, there is less hydrochloric acid in the stomach (Krause (116)). This has been correlated with the idea that after gastroenterostomy, there is less stasis of food in the stomach. But, in most cases, the reason must be that the acid is neutralized by backflow of alkaline juices (Katzenstein (117), Schuller). In addition to this, so to speak, test tube neutralization, experiments with Pawlow's miniature stomach (Katzenstein) have shown that the presence of small quantities of intestinal juice results in a reflex inhibition of hydrochloric acid production. According to Kausch and Kaplan (118), this backflow of intestinal fluid ceases during subsequent years. This does not seem to be the rule, however, for Schuller could not find increased hydrochloric acid in his patients when he re-examined them some time after operation. As soon as the alkaline intestinal juice enters the stomach, pepsin digestion is interrupted, for this enzyme digests only in the presence of acid, and a trace of alkalinity destroys its ferment activity. But the digestion of protein in the stomach is not completely lost because trypsin in the backflowing pancreatic juice takes over this function (119). Trypsin is much less sensitive to changes in reaction than pepsin, and its digestive power for protein is only checked and not completely destroyed (Katzenstein). The other two pancreatic enzymes, diastatic and lipolytic, are also resistant to acid and thus, after gastroenterostomy, digestive processes take place in the stomach which ordinarily occur only in the bowel. Carbohydrates are broken down by the diastase, fats by lipase and bile. The rennin from the stomach is replaced by a similar enzyme from the pancreas. Altogether, the absent gastric digestion is compensated so well, that no changes are demonstrable in the total metabolism of either nitrogen, carbohydrates or fats (Heinshimer (120)). This latter may, however, depend partly on the fact brought out by Dagaew's investigations (121), *viz.*, that the passage of food through the small intestine is considerably slowed. Thus, the food is probably comminuted and absorbed in an approximately normal manner, before it enters the colon.

But since after gastroenterostomy and pyloric closure, the food does not pass over the papilla of Vater, how are the pancreas and the gall bladder stimulated? The principal stimulus to pancreatic secretion is the secretin, which is formed from prosecretin by hydrochloric acid, is absorbed from the intestinal wall and carried to the pancreas by way of the blood stream (Bayliss and Starling (122)). Since prosecretin is present in the jejunum also, the flow of pancreatic juice after gastroenterostomy is easily understood. But normally, there are a number of other substances, chiefly soaps and oils, which act as direct stimuli to the pancreas, probably through nervous paths (see Cohnheim and Klee (123)).



According to the investigations of Bickel (124), who extirpated the duodenum in a dog and sutured the papilla of Vater to the abdominal walls as a fistula, these reflexes may also arise in the jejunal mucosa. This holds good for both pancreatic juice and bile. For the digestion of any sort of food, it is principally the bile which has been in the gall bladder and the bile ducts, and not newly formed bile which is important (125). Schoemaker obtained the same results (108); he observed, after closure of the pylorus and gastroenterostomy in dogs with fistulæ, the regular action of these reflexes.

Katzenstein (117) (p. 138) assumes from his investigations, that impulses from the stomach may also give rise to pancreatic secretion and bile flow. His experiments are, however, open to doubt, since the pylorus was not cut through and a flow of stomach contents into the duodenum can never be excluded after simple gastroenterostomy.

But there is still another possibility regarding the secretory mechanism of bile and pancreatic juice. Kelling (126) observed a considerable backflow of food into the duodenum after resection of the stomach with duodenal fistula. In such cases, the food flows over the papilla of Vater and may thus directly stimulate the glands.

Casagli's (127) histological investigations have shown that when the duodenum is eliminated even partially from the digestive processes there results a sclerosis of the submucosa and of Brunner's glands, as well as a thinning of the musculature.

Regurgitation of bile and pancreatic secretion into the stomach has been observed when patients vomit for a long time after operation, as in the condition which occurs particularly in so-called vicious circle, of which we will speak later. It was believed on account of this, that the vomiting itself and the rapid downfall in such patients was a result purely of the entrance of bile and pancreatic secretion into the stomach. This idea was pursued in many experiments, and even though our conception of the cause of vomiting in vicious circle has undergone change, these studies not only have historic interest, but they give us a key to understanding many lesser disturbances after gastroenterostomy.

Chlumsky (128) cut through the intestine of dogs just below the duodeno-jejunal plica, and sutured both openings to different places of the stomach, thereby leading duodenal fluid into the organ through one opening and allowing its emptying through another. It is true the dogs did not vomit, but they died after a few days, and showed no satisfactory cause of death. They displayed great thirst and at autopsy, the intestines were filled with dark brown fluid feces. The introduction of bile by anastomosis of gall bladder and stomach was followed by recovery of the animals (129), but death occurred again in a manner similar to that de-

scribed above, when the bile was eliminated by a cholecyst-enterostomy and only pancreatic fluid was allowed to enter the stomach. Different results were obtained by Steudel (130) who varied this experimental method by sectioning the bowel at the same place, and then closing the duodenum, so that its contents had to pass periodically through the pylorus. Chlumsky explains these latter results by assuming that a periodic discharge of bile and pancreatic juice is less harmful to the dogs than a continuous one. But the conclusions which Chlumsky draws from his own work are certainly too far reaching. The fact that a dog dies after an operation on its stomach proves very little, because dogs generally do not stand laparotomies very well (Pawlow, Cohnheim (9)), particularly when the operation or even the manipulations include the pylorus. Often enough, dogs die with exactly the same symptoms and autopsy findings as Chlumsky describes, after entirely different operative procedures on the gastrointestinal tract, *e.g.*, simple gastroenterostomy (author's own observation). Furthermore, Kelling (131) succeeded in keeping a dog alive and perfectly healthy for a long time after an exactly similar operative technic. While it is true that more critical analyses are needed here, perhaps with the help of fistulae, it nevertheless cannot be denied after these experiments, that backflow of bile and pancreatic juice may under certain conditions cause trouble. According to Stuber (132) a backflow of trypsin in animals leads to the formation of gastric ulcers, which do not appear to differ from those found in man in whom these have not as yet been described. The possibility must, however, be kept in mind. Furthermore, apart from changes in gastric digestion, a mixture of hydrochloric acid, bile and proteins, leads to the formation of bile acid salts, which are very difficult for enzymes to attack (21).

On the whole, regurgitation produces no trouble in man, but now and then, individuals appear who for a longer or shorter time after gastroenterostomy have eructations of bile, nausea, and other symptoms which must be attributed to this condition (133). Why trouble should occur in some individuals and not in others with the same pathological conditions cannot be answered with certainty. Psychic, or if you like, neurasthenic processes may play some role.

As stated, this backflow is observed principally in connection with the so-called *vicious circle*, or as it is probably better called by Peterson (4), gastric ileus. This very undesirable complication of gastroenterostomy occurred even at the cradle of this very beneficial operative procedure. Indeed Wolfler (134) in his first communication on gastroenterostomy reported such a case. Physiologically, quite a number of different conditions are included under this name (135). In the first place, a backflow of duodenal contents may occur *through an open pylorus*, secondly, duodenal

contents in larger quantity may flow into the stomach *from the proximal loop*. In the third place, stomach contents *may enter the proximal loop*, instead of the distal, flow backwards through the duodenum and pylorus into the stomach, then into the proximal loop again and so on (vicious circle). With a closed pylorus, combinations of two and three would occur. Fourth, a backflow of intestinal contents *from the distal loop* has been observed as a cause of vicious circle.

The reasons for gastric ileus after gastroenterostomy are found in technical errors, which have gradually become so well known, thanks to the studies and experiments of numerous authors, that this complication is a rarity at the present time. Since it occurs much more frequently after anterior gastroenterostomy on account of the torsion and compression of the jejunal loop, the posterior operation is preferred. Furthermore, a long loop favors antiperistalsis, therefore it is made as short as is consistent with reaching comfortably from the duodeno-jejunal plica to the place of anastomosis (136). The loop cannot therefore be of the same length in each case, but must be longer with a deeply situated, dilated stomach, than with one of normal size (4). Even this consideration does not always hold, for the stomach may change its size after operation and *spur formation*, larger than ordinarily occurs, will result. Such a spur acts like the dam in a mill race and vicious circle is often the result.

Finally, with the pylorus wide open, and a failure of the sutures in the mucosa the gastroenterostomy may shrink and a vicious circle arise from this cause (128). All these difficulties in evacuation are found more frequently in relaxed than in normal stomachs.

This is not the place to discuss the methods which have been devised, to obviate vicious circle (see Tavel (135), Peterson (4), and others). Their principles explain themselves from what has been said above. Summing up our present knowledge, the so-called *vicious circle is a true, high situated ileus* resulting from a more or less complete *mechanical closure* of the bowel. The enormous dilatation of the duodenum which has been described in this condition can be explained by the same considerations (137). We will discuss the general pathological physiological consequences of ileus, the causes of death, etc. in a separate chapter.

The *diarrhea* which is occasionally observed after gastroenterostomy has been explained (138) in certain cases by the sudden entrance into the bowel of decomposed material which had stagnated in the stomach before the operation, *e.g.*, in carcinoma (139). [This must occur very seldom because in well appointed clinics a gastric lavage before operation is routine. This, however, may fail to remove some contents.] Where such a condition cannot be found, an explanation is more difficult. In these cases, an assumption is made based on investigations of Matthes (97) who found

that the injection of gastric juice into the ileum causes severe enteritis and that hydrochloric acid when injected into the jejunum produces diarrhea (131). This idea has not received general recognition, chiefly because hypoacidity is found much more frequently after gastroenterostomy on account of the backflow of alkaline intestinal juices. Conversely, Schuller calls attention to the diarrhea which occurs with ordinary anacidity and believes there is an analogy in gastroenterostomy. This question has, however, not yet been answered.

[Diarrhea so severe that it ended fatally has been seen after gastroenterostomy (140). With the idea of gradient in mind (Alvarez (61)), the process can be attributed in some cases of gastroenterostomy to a rapid outpouring of food which enormously raises the tonus and irritability of the upper intestine, perhaps by the very distention, and leads to a hurried passage of the contents.]

The communications reported by roentgenologists regarding the progressive movement of the contents through the ileum and colon after gastroenterostomy are contradictory. A number of authors report a slight slowing of the passage through the ileum (Schuller (103)). Others state that the shadow of bismuth appears at the left flexure in five hours (141). Doubtless the subjects investigated (human patients), showed too many individual differences, so that slowing or acceleration of peristalsis must be correlated with factors other than gastroenterostomy.

Another very disagreeable complication of gastroenterostomy is the *development of ulcers* at the site of the anastomosis to the jejunum. The similarity of all ulcers in the region of the stomach and intestines, and the numerous investigations to determine how this condition arises will be discussed in the paragraph on gastric ulcers, but certain peculiarities of jejunal ulcers may be pointed out.

According to our present viewpoint, these, like all other peptic ulcers, are formed by the digestion of an intestinal wall previously devitalized by injury. According to Van Roojen (142) in 41, out of 56 cases, they were located at the gastroenterostomy opening, in two cases, at the place of Braun's anastomosis; while the remainder were scattered in different parts of the bowel. On the whole, they are rare.

[In the experience at the Lankenau Hospital they were found in about 2 per cent. of cases of gastroenterostomy.]

Gasset believes they occur more frequently after anterior gastroenterostomy (143), but according to von Haberer (144), they are more frequent after the posterior operation with short loop. They are especially dangerous because they perforate readily, usually into the free abdominal cavity since fixed parenchymatous organs to which they might adhere and which are in the neighborhood of ordinary gastric ulcers, are



distant. Isolated cases of jejunal ulcer have also been observed without previous gastroenterostomy (von Roojen). In one of the cases an extensive burn of the skin was the cause of death. From the very beginning there was a difference of opinion as to whether they resulted from the entrance of gastric juice into the bowel, since the bowel is not normally adjusted to acid gastric juice, or whether other factors also came into play. Katzenstein (145) and Kathe (146) isolated loops of intestine in the stomach of dogs but retained their connection with the mesentery and thus disturbed the nutrition as little as possible. They found that intestinal mucosa has no resistance to the digestive power of the gastric juice, and is completely dissolved in a short time, but gastric mucosa implanted into the stomach shows a much greater resistance. Katzenstein concludes from his experiments that the latter contains an anti-enzyme which is absent in the mucosa of the intestine. More recent investigations (147), however, indicate that these results may have another explanation. The digestion of the loops of intestine as found by Katzenstein is due entirely to nutritional disturbances resulting from an inadequate circulation.

The doctrine that specific protection against autodigestion is possessed only by the gastric mucosa cannot be accepted in the form elaborated by Katzenstein. Among other ways this was shown by the investigations of Titze (148) who sutured omentum as a protection into an injured gastric wall. He observed no digestion at all and this method has gained considerable favor in operations for perforating gastric ulcers.

Nevertheless, it is doubtless correct that the jejunal mucosa is very sensitive to hydrochloric acid for when Matthes (149) injected hydrochloric acid and pepsin into dogs through a fistula into the intestine, he observed that the acid first killed the cells and then the digestive action of the pepsin began. He could obtain extensive destruction of bowel mucosa in this way. Matthes is therefore still of the opinion that the jejunum can be so injured by an hyperacid gastric juice as to cause the development of an ulcer. The importance of hyperacidity in the formation of jejunal ulcers is further illustrated by statistics. Von Roojen found hyperacidity present 21 times in his cases; it was normal or below normal 12 times; and Patrion (150) reports 13 cases of hyperacidity in 18 jejunal ulcers. Consequently jejunal ulcer is rare after gastroenterostomy for carcinoma because hypoacidity is usually present in such cases. Ordinarily the gastric juice, which comes in contact with the bowel wall, is not strongly acid, because, as stated above, in the majority of cases, it is neutralized by the backflow of bile and pancreatic juice.

Doubtless, this is a considerable protection for the jejunum, and it helps explain why jejunal ulcer is more common when those operative



methods are used which either prevent or diminish this regurgitation. After Braun's anastomosis (151), Neuhaus (106) could demonstrate that no bowel secretions can re-enter the stomach, and this is also true of Roux's "Y" anastomosis (statistics of Von Roojen: compare this with Von Haberer (144)). Exalto performed gastroenterostomies in seven dogs and fed them mixed food and hydrochloric acid daily for some time without finding jejunal ulcers, while, of seven other dogs operated by the "Y" method and fed similarly, five died of perforating jejunal ulcers. Bickel's investigations (124) yielded the same results. He extirpated the duodenum in a dog and deflected bile and pancreatic secretions to the exterior. This animal also died of perforating jejunal ulcer. The back-flow of bile and pancreatic secretions into the stomach evidently can neutralize even a high grade hyperacidity, and thus make it harmless to the jejunum; for to mention another experiment (Borszeky (109)) performed gastroenterostomies on 12 dogs and gave them two tablespoonsful of strong hydrochloric acid daily for three months. He then found a fatal perforating jejunal ulcer at the gastroenterostomy site in only one dog.

Although we have seen that the principal reason for the formation of jejunal ulcers is the action of hydrochloric acid on the jejunal mucosa, the fact must not be overlooked that jejunal ulcers may occur, though rarely, even in diminished or absent acidity (Mikulicz, Kocher, Heidenhain and many others (107)). In these cases another factor must be considered, namely, that the vitality and resistance of the jejunal wall has been injured by some substance other than hydrochloric acid. Naturally, such injuries occur frequently to the jejunal epithelium during the operation and especially at the place of the gastroenterostomy opening where the mucosa may be injured by the pull of the sutures or the pressure of a Murphy button. In discussing the histology of the repair of wounds of the stomach, it was pointed out that the mucosa of the intestine frequently breaks down at that place, so that healing proceeds by granulation. Such unprotected wound surfaces offer an especially good point of attack for the digestive action of the gastric juice, and statistics actually show that ulcers are most frequent at the opening. According to Haberer's (144) experience, however, they are, as a rule, not situated along the line of suture, but are usually distal to it.

The importance of mechanical injury to jejunal mucosa as a cause of ulceration, is very well brought out in a communication by William Mayo (152). He observed only three jejunal ulcers among a large number of gastroenterostomies—one was caused by a Murphy button inserted three and a half years before, and still in situ; the second had formed on the floor of a suppurating hematoma in the transverse meso-colon; and in the third, an infected silk suture was found. In reference to the last observation,

the danger of silk as a suture material for the mucosa is especially emphasized in the English (Wilkie (99)) and French literature. In a recent publication, von Haberer (144) also expressed the opinion that silk thread, by daily friction, produced an ulcer a short distance from the line of sutures, and after observing this case, he infers that the jejunal mucosa may be so irritated by the mechanical action of food that ulcers result.

The motor activity of the stomach is influenced to a much greater degree by *pyloric resection* than by simple gastroenterostomy. Three years before it was first done in man (Pean (1879)), Gussenbauer and Winiwarter had shown that the dog could withstand removal of this part of the stomach. These experiments, as well as those done as early as 1810 by Merrem, pathfinding though they are, give us only a general idea of the effects on gastric function. Only in recent years have accurate investigations of the activities of the resected stomach been made with the help of the x-rays and fistulæ (von Mering, Schuller, Dagaew, Kaplan and others (153)). Von Mering found no change in the evacuation time when he resected the pylorus and sutured the duodenum to the stump of the stomach. His statements, however, are only very general. The motor function was examined more carefully by Dagaew and later by Kaplan on the same dogs in the London Institute of St. Petersburg. These authors found a slowing of gastric evacuation which remained unchanged for years. This is very varied and is less after operation by the first method of Billroth than after the second. The contraction of the attached small intestine maintains periodicity of gastric evacuation and also slows it by the resistance of its pendulum movements (Dagaew). If other factors were inoperative, the resected stomach would empty rather more quickly than the normal, for the reflexes arising in the bowel and ordinarily acting on the pylorus, now act on the fundus. Anatomically, there is of course no sphincter developed, but von Mering found that by introducing a finger, the gastric opening into the bowel closed under stimulation just as perfectly as when the pylorus was preserved.

Investigations (Gocke (154) and others) have shown that conditions are more favorable in man than in animals probably on account of his upright position, and quite normal evacuation of the stomach may be present even with Billroth's second method. According to Gocke, the evacuation time depends on the position of the remainder of the stomach. The steeper this is, that is, the shorter the remaining part of the greater curvature, the quicker the stomach empties itself. This explains the contradictory results obtained in animals and in man, as recorded by Schuller (155). In some of his patients, all of whom were operated by Billroth's second method, the evacuation took two and one half to four hours, *i.e.*,

it was approximately normal. In others, it was considerably accelerated. In one case, three years after operation, the stomach was quite empty in five minutes. In patients who were examined more than once, it was found that the evacuation time varied on different days; for instance, the individual whose stomach emptied in five minutes, returned two months later and at that time retained the chyme for one hour after eating. According to Schuller, the cause of this irregularity is chiefly mechanical, and is influenced by gravity since the actual gastric motor, the antrum pylori, has been removed. Compressions and kinkings, as well as shrinking of the attached bowel may result. Generally speaking, the same considerations regarding backflow of bile and pancreatic juice that were discussed under gastroenterostomy, hold good for resection.

When the fundus was resected in animals, Kaplan (118) could demonstrate an accelerated gastric evacuation which was practically independent of the size of the resected portion.

The results, following *transverse resection*, have been investigated very carefully from all standpoints both in animals and in man by Kirschner and Mangold (54), Gocke (154), von Redwitz (156), and others. Kirschner and Mangold could show that such an incomplete section of the sympathetic and vagus fibres as occurs in this resection has no noteworthy effect on the antrum movements and reflexes; there is an outspoken autonomy here. According to von Redwitz, if a large part of the fundus is removed, the mixing of food is interfered with, but the emptying of the liquefied gastric contents into the duodenum is less affected. Furthermore, transverse resection has also no appreciable influence on the quality of the gastric juice but the food, especially proteins, tends to remain longer in the stomach since the diminution of secretion to digest the food is proportionate to the amount of stomach removed. The numerous x-ray studies after transverse resection in man, have not yielded entirely similar results (157). Kummell could observe a deep spastic contraction at the site of the resection. Faulhaber and von Redwitz found only a shallow contraction in this area, caused perhaps by the sutures. According to Gocke, the peristaltic wave does not pass across the area of resection. But it is especially the findings regarding gastric evacuation which vary. In some cases rapid evacuation was observed; in others, it was normal. The experiments of Kaplan, mentioned above, seemed to support the statement that accelerated gastric evacuation results if much of the fundus is resected. Von Redwitz does not share this conclusion, but believes with Gocke that the rapidity depends on the shape of the remaining part (see above). On the other hand, Perthes believes that rapid gastric evacuation can only be explained by assuming that the pylorus remains open. This, however, is not the case according to the animal

experiments of von Redwitz. The relation found by Perthes between the rapid evacuation of the stomach and the appearance of hunger sensations, is very interesting. Sense of hunger was absent when a six hour residue remained in the stomach. Other investigators, like Gocke, could not demonstrate any parallelism between gastric evacuation and hunger sensation and the findings seemed to point to the conclusion that hunger sensation is not dependent on the presence of the stomach. According to Thoma (L. R. Muller) (158) these sensations are brought about by a deficit of nutritive substances in the blood, the presence of which normally quiets the hunger center in the mid-brain.

[See page 147 and Carlson's article in "Harvey Lectures" 1915-1916.]

*Total resection* is now being performed more frequently since a large number of surgeons have abandoned simple gastroenterostomy for the treatment of peptic ulcer distant from the pylorus. The number of published cases, about forty, is probably not the real figure (159). The first of such investigations was made by Czerny in dogs (Kaiser (160)). One of these animals which lived five years after the operation, was later examined by Ludwig, *i.e.*, Ogata. This animal has gained a certain fame in literature, which, however, is not quite justified, since at the autopsy it was found that a piece of stomach had been left at the cardia and had expanded into a small bag. In the dog reported by Monari (161), a strip of stomach remained, although distinctly smaller than that in Czerny's dog, and at least no new gastric pouch formed from it. The same is true of the dog of Matthes-Grohe (159), but Dagaew (121) succeeded in doing an anatomically proved total gastric resection uniting the esophagus to the duodenum. DeFillippi (162) could not demonstrate any changes in metabolism in Monari's dog which was similarly operated. At autopsy, it was shown that both the lower part of the esophagus and the duodenum were distended like a pouch. The enlargement of the cardiac end of the esophagus results probably from the section of vagus fibres. Enlargement also occurs in man as described by Cohn (163) in a case operated by Unger (164). Accurate analyses of the processes of digestion have been made in a few of those cases in which good results followed the operation (159) and these have shown that neither the sensation of hunger nor of satiation (Cohn) is felt although a peculiar pressure sensation in the abdomen warns them when the upper portion of the bowel and the esophagus are filled, that they must stop eating. The food remains for a very short time in this bag-like dilatation of the esophagus and then is transported through the intestines very slowly, taking 24 hours to reach the cecum; but the statements regarding hunger sensations in total or subtotal gastric resection vary quite considerably. A man operated years ago in this clinic shows only one discomfort, and that a



continuous sense of hunger and an enormous quite untimely appetite (see also transverse resection).

The slow passage through the intestines should probably be considered as due chiefly to vagus resection. At least, it cannot be deduced from Ogata's experiments (165), that the presence *per se* of food which had not been in the stomach, slowed its passage through the small intestines. His work was done on dogs which he fed through fistulæ in the small intestine, and thus excluded gastric digestion. Unger's patient was very constipated after the operation. This also may possibly be considered due to the cutting of vagus fibres (Cohn). In a case of Schlatter (166) (the first successful gastrectomy (1897)) although no constipation resulted, huckleberries, given as a test substance, did not appear in the stools until 72 hours after ingestion.

Now what functions must be assumed by the small intestines after total gastric resection? We have seen above that the chief function of the stomach is to act as a mechanical reservoir in which food is liquefied, that is, brought to a consistency most useful to the bowel. At the same time, it regulates the supply and admits only small quantities at a time. The slight dilatation of the esophagus cannot receive consideration as a substitute. We must, therefore, give finely comminuted food in small amounts to facilitate the work of the bowel. We have seen, in discussing gastroenterostomy, that the digestive processes of a chemical nature can be carried out perfectly by the pancreatic juice and the bile. Pepsin is replaced by trypsin and in a similar manner the other less important enzymes, including the milk curdling ferment, are present in pancreatic and intestinal juices (167). Consequently there is nothing to fear in regard to the chemical splitting of food and, really, the only anomaly demonstrable is the absence of bile acids in the feces, which must be due to the lack of hydrochloric acid. This conclusion was reached after numerous examinations of urine and feces made when food was given through a duodenal fistula (Ogata (165)) when the entire stomach was resected as in the dog of Monari (de Fillipi) and in the human gastrectomy of Schlatter (168). In the latter case, no microscopical abnormality was found in the feces, nor were decomposition products such as scatol or indol, detected in the urine or in abnormal amounts in the feces in spite of the absence of the disinfecting power of the stomach (see also Ssolwjew (169)). It follows when complete compensation does not occur in a patient (Cohn), but disturbances in the evacuation and the condition of the feces are present, that these must necessarily be charged to secondary factors (severe anemia, cachexia, etc.).

In examining the histories of patients who have had a total gastric resection, it is often found that the patients vomit. This of course in



the absence of the stomach attracts attention and two types must be differentiated, one similar to that occurring in cardiospasm in which stagnating masses in the lower end of the esophagus are emptied without nausea (Cohn), and second, an actual vomiting of the food which has been in the small intestine (Schlatter).

Even when, as stated, the small intestine satisfactorily takes over the functions of the stomach, evidences of this abnormal activity are left behind principally in the form of atrophy of the intestinal mucosa (Dagaew). It is interesting that such a change may occur in the duodenum even after simple gastroenterostomy (Casagli (127)). The small intestine, therefore, seems more sensitive to all these operative procedures than examinations of the metabolism would indicate.

When the resection is not quite complete, a dilatation of the stump may occur in the course of time. The duodenum also dilates, and a gastric pouch finally results, which, in Schuchardt's case (170) almost approached the original stomach in size.

*Gastric, duodenal and jejunal ulcers* (see above) are, according to our present viewpoint, not specific diseases. For their formation, two interacting factors must be considered. The first is injury to gastric and intestinal cells which must always occur before the second factor, namely, the digestive action of gastric juice, can operate.

Without previous injury the *stomach wall is not digested*. A very large number of hypotheses have been proposed and investigated to explain the protective power of the mucosa against self digestion. In the first place, mucus, probably through its mucin content, acts as a protection by covering the epithelium (Roux and Riva (171); Claude Bernard); (Klug (172)); on the other hand, Danilewsky assumes the presence of a so-called anti-pepsin (173). Kaufmann demonstrated a consistent lack of mucus in gastric ulcer (174), but it can be shown experimentally that this substance does not give absolute protection. Payr, for instance, produced typical ulcers by causing thrombosis of gastric vessels even when the distribution of mucus over the epithelium was not changed in the least.

Pavy's old theory that the blood circulating in the gastric vessels becomes richer in alkali because the gland epithelium deprives it of the chlorine to manufacture hydrochloric acid enjoyed general recognition for some time, but no proof has ever been offered for its truth. On the contrary, Edinger (175) has shown that the acid reaction is present not only on the surface of the mucosa, but also in the deeper layers. This rather elementary theory can therefore be discarded and search for the immunity to digestion of the uninjured stomach wall must be directed to properties possessed by the cells themselves. The question is simply this: Is resistance to digestion a general property of all living uninjured cells

as Hunter believed (176) or is it a specific property of gastric epithelium? Hunter's teaching seemed disproved by the famous experiment of Claude Bernard (177) in which he placed the thigh of a living frog through a fistula into the stomach and found that it was promptly digested. Pavy observed the same result with a rabbit's ear. These experiments, however, do not demonstrate the fact for which they were designed; for in both cases it was not the living, but a previously devitalized protoplasm which was digested. This is shown especially in the well planned experiments of Matthes (178), who demonstrated that by these methods, the hydrochloric acid of the gastric juice, acting as protoplasmic poison, kills the cells before they are digested. In Claude Bernard's and Pavy's investigations this injurious action of the acid was probably further favored by the circulatory disturbances incident to the ligation of the frog's thigh or the rabbit's ear. "In the presence of living uninjured tissue, digestive enzymes are inactive" (Matthes).

The question has now been concentrated to this: Why does hydrochloric acid produce no injury to the gastric mucosa? Matthes' investigations give at least a partial answer to this. He found that a natural gastric juice with a high acidity digested proteins more quickly and thoroughly than an artificial one of even lower acidity, but acted less injuriously on living tissue. Doubtless this depends on a partial neutralization of the hydrochloric acid by albumoses and peptones and also, perhaps, on protection by the mucus so that natural gastric juice seems less injurious than its content of the acid would indicate. This restriction of the action of the acid in the stomach cannot, however, be the only reason why the mucosa is normally uninfluenced, for then it would be difficult to understand why gastric juice which has had no influence on mucosa, digests the skin over which it flows from an open gastric fistula. This experience, so familiar to all surgeons, therefore obliges us to assume some sort of a specific protective property inherent in gastric epithelium. This must be accepted, simply as a fact, without any clear explanation.

Other studies of Matthes have shown that the other tissues of the body vary in their susceptibility to the action of hydrochloric acid and it seems that the stomach wall itself is not absolutely protected. He states that in dogs, ulcers produced by trauma heal more slowly if about 50 c.c. of 0.56 per cent. solution of hydrochloric acid is given by mouth on an empty stomach. Naturally, these investigations did not remain unchallenged (Neumann (179)). The objection was made that such a small quantity of hydrochloric acid hardly increased the per cent. of acid in the stomach contents. But this objection may not be valid, for as stated above, artificially introduced hydrochloric acid is more irritating than the natural, because the latter is partly bound.

Kehrer (180) performed the following experiments with dogs on the same problem. After cutting the biliary and pancreatic ducts, he diverted these secretions into lower bowel segments. The chyme remained acid for a longer period in the duodenum, the pylorus remained closed and the fluid in the stomach became strongly acid. As a matter of fact in a few cases he did obtain ulceration of the gastric mucosa. But this does not necessarily mean that high acidity should be considered particularly important, for, according to the newest statistics, hyperchlorhydria is a frequent, but by no means constant accompaniment of gastric ulcer. In many cases it is brought about by pyloric stenosis (see above) and as Virchow (181) emphasized long ago, such a hyperchlorhydria, without local injury, would give rise to only a gastromalacia and never to a circumscribed ulcer.

Matthes' experiments practically prove that the stomach does not digest itself because of a special resistance to hydrochloric acid, but its immunity to pepsin must also be taken into account, since large experimental lesions of the mucosa quickly cicatrize and never lead to typical ulcers. This idea was again brought into prominence when so-called antipepsin was first demonstrated in the gastric juice and blood. All we know of this antienzyme is that the activity of pepsin is frequently checked and that quite different substances may be involved. From certain properties which it exhibits it may be assumed that it does not belong to the actual antibodies. Such pepsin inhibitory substances occur in the most diverse, and in the lowest forms of life, as for instance, in bacterial extracts (Krasnogorski (182)); so that there is nothing specific about its presence in gastric juice or in intestinal parasites as it was once believed. Some surgeons, however, are still of the opinion that gastric ulcers must be attributed to an absence of antipepsin in the stomach wall (183). Katzenstein was one of these and to prove this view, he transplanted sections of intestine, spleen, omentum, etc. into the stomach and found, without exception, that they were digested; implanted stomach wall, however, was not affected. Furthermore, he could produce chronic perforating gastric ulcers in animals by destroying the antipepsin. The same objections as those mentioned in connection with Claude Bernard's experiments hold good for this first group; it was not a question of digesting living intact tissue, but tissue with its nutrition disturbed.

Other authors (184) had already obtained contradictory results from similar experiments before Katzenstein's work, and Licini (185) and Hotz (186) who repeated them with similar technic, but with especial care of the nutrition of the implanted part, found no digestion of either the spleen or intestine. On the other hand, Best (186) has recently obtained opposite results again. Obviously in experimental methods of such a nature,

negative results have more weight than positive, because disturbances of nutrition can never be excluded with certainty. In his second group of experiments, Katzenstein injected dilute hydrochloric acid into the gastric wall or the blood stream to weaken the antipepsin, which supposedly acts only in alkaline media, but results by this method may be also explained on different grounds. The injection itself injures the tissues and this injury may be increased by reflex vessel cramp (see later) after the acid is introduced into the blood stream.

Thus the theory that the protection of the stomach against auto-digestion resides in an antipepsin, and that a diminution of this substance in the stomach wall is followed by gastric ulcer, is yet to be proved.

Stuber (132) recently expressed another opinion; that it was not the gastric juice which attacked the stomach, but trypsin, and that the pancreatic juice entered the stomach through a "neurogenically insufficient pylorus." He attempted to prove the correctness of this theory by experiments on animals. In five dogs, he obtained multiple gastric ulcers, some of them calloused, by partial resection of the pyloric muscle and the administration of sodium bicarbonate. These experiments should be repeated and their merit determined since they are of great importance, especially in the treatment of gastric ulcer.

The primary factor in the formation of gastric ulcer is injury to gastric or intestinal mucosa. There is doubtless a certain analogy to leg ulcers. Wounds on other parts of the body surface tend to heal without difficulty, but wounds on the lower leg from the ankle to the middle, are often very stubborn. Similarly, according to the experiments of Ribbert (187) artificially produced ulcers in the stomach, provided they are of sufficient size, show no tendency to heal, even in healthy animals. Nutritional disturbances following insufficient blood supply, are factors of the highest importance for consideration (Virchow (181)). Many unsuccessful attempts have been made to injure the nutrition of the stomach wall by ligation of vessels, sufficiently to produce a typical ulcer (187). Disse (188) may be consulted regarding the blood vessel supply of the gastric mucosa. According to Braun (Alberts (189)), four-fifths and more of the gastric vessels may be ligated without danger of gangrene, but Fibich (190) obtained progressive ulcers of the mucosa by the ligation of arteries and the excision of a portion of the mucous membrane with cauterization of the base. Generally speaking, however, the anastomosis of the gastric vessels is sufficiently free to provide adequate blood supply so that even artificially produced defects of the mucosa with simultaneous ligation of the arteries, heal easily. Clairmont (187) in attempting to repeat Fibich's experiments could not confirm his results. Since these experiments failed, the logical procedure was to interfere with the gastric circulation through



capillary thrombosis, especially since Panum had shown (191) that the introduction of wax pellets, etc. into the femoral artery against the blood stream was followed by ulceration in the stomach and intestines. Cohnheim (192) injected chrome alum into the gastric artery and found "large ulcers with steep margins and perfectly clean bases in all the animals which died or were killed within one or two days." Payr (193) by the injection of dermatol, India ink, and particularly formalin, obtained typical ulcers, but they were also progressive so that they were very similar to those found in man. Ulcers produced by ordinary embolism healed very quickly, and this latter fact is essentially different from human gastric ulcers. But since Payr always obtained progressive ulcers by the injection of formalin, it seems to show that if the vascular injury is extensive enough, ulcers will form. Hauser (194) had already assumed this on the basis of his pathological anatomical studies. V. Redwitz (195) also after extensive histological examinations stated that thrombosis is very frequent in the region of an ulcer. Of course the question immediately arises, are these thromboses primary or secondary? Does pathological anatomy give any good reason for believing that thrombosis or embolism precedes gastric ulcer, as they do when the nutrition of the gastric wall is shut off experimentally? As a matter of fact, a number of such cases have been reported in the literature. Thus v. Recklinghausen (196), and later Merkel (197) have described cases of ulcer following embolism, and at least one case of hemorrhagic infarction of the stomach wall has been reported by Hauser (194). Such embolic showers are usually the result of an endocarditis, or of an extensive venous thrombosis, as in v. Recklinghausen's case. They seldom offer opportunity for surgical interference on account of the grave general condition of the patients.

Those ulcers observed following resection of the omentum belong perhaps to the same group, but they deserve considerable clinical attention (198). The keen controversy which was waged some years ago, as to whether the emboli following resection of the omentum occurred only in the presence of infection has now been settled. Infection is not necessary, but in its presence, thrombosis and ulceration are probably much more frequent (see also Sprengel (199)). It is useful to differentiate those cases of hematemesis which occur post-operatively and in which the operation played the chief role, from those occurring in non-operated cases in which the offender is in all probability an infection, particularly of the peritoneum. This has not been done in the literature, and it has added another confusing factor in this very difficult field. After ligation of the omentum, thromboses have been found, not only in the vessels of the stomach but also in those of the liver and they have been accompanied by focal necroses. This seems to show that a retrograde process occurs in the region of the



portal vein. The underlying conditions have been studied very carefully by Payr (193) who produced thrombosis by freezing the peripheral parts of the omentum, and then followed its progress by the injection of foreign bodies. Experiment thus showed him that "emboli in the course of the veins could move toward the stomach and produce all the changes which had long been attributed to them."

This retrograde embolism is favored in the first place by the relatively straight course of the veins, and further by the fact that according to the investigations of Hochstetter (200) no valves remain in the veins of individuals over 20 years of age. By a like reasoning, the presence of valves in children is said to prevent post-operative gastric ulcers. The researches of Payr have been checked by the investigations of Yatsushiro (201) who concluded that Payr obtained retrograde embolism simply because he used too high pressure in his injections. Finally, it is believed by some, especially by internists, that it is not a question of embolism in post-operative ulcers, but reflex vessel spasm (see later). It is a fact that embolism and thrombosis are not found frequently enough at autopsy to account for the very often severe hematemesis ("vomito negro").

Nitsche (202) has reported a case of hematemesis following appendicitis, which showed microscopic necroses and hemorrhages in the mucosa three hours after death. These he attributes, in the absence of thrombi, to an excretion of toxic substances by the gastric glands, just as alkaloids, for example, are excreted. This excretion "injures" the glands, and would be of course a special form of septic injury, not embolic, but toxic. In other cases, a so-called "parenchymatous" bleeding is dealt with (Reichard (203)), of which we know only that it occurs in certain family groups. Ulcers are not present nor do they occur in "bleeders," though trauma may initiate them.

Among the pathological anatomical observations which are said to show circulatory and therefore nutritional disturbances in the gastric mucosa, the erosions following passive congestion, following certain brain affections, and vomiting (Orth (204)) may be mentioned. Finally, we may also consider those in individuals with a more or less extensive arteriosclerosis and degeneration in the vessels (Kaufmann (205)) and those following traumatic changes in the blood supply. It must require quite an extensive destruction of blood supply either through laceration of the vessels or reflexly by vessel cramp to produce an ulcer after trauma, because we know from numerous experiments that in the absence of extensive injury to vessels artificial defects in the mucosa show a pronounced tendency to heal. In connection with observations in Leube's clinic, Ritter (206) studied the effect of blows delivered through the abdominal walls on the stomachs of dogs. He found that there resulted mainly

"a complete separation of mucosa from submucosa, with hemorrhage into the latter" and slight bleeding into the other layers of the stomach. He did not obtain a true ulcer. Chronic traumatism, the importance of which is very variable in the formation of an ulcer, may be caused by tight lacing, but it is very difficult to determine the significance of this factor in relation to gastric ulcer. Displacement of the position of the stomach, as in diaphragmatic hernia (207) may also lead to ulcer by disturbances of nutrition. Furthermore, injuries of every possible kind may affect the inner surface of the stomach and produce a defect in the mucosa. Decker (208) by repeated introduction under the mucosa of fluid warmed to 50 degrees, obtained hemorrhages and deep loss of tissue. It is a well known fact that cooks suffer comparatively frequently from gastric ulcer perhaps because they often taste very hot food, and ulcers are also quite frequent in mirror workers, metal workers, porcelain workers and others who swallow sharp particles. Doubtless, in the last mentioned cases, the factor of chief importance is vessel spasm rather than injury to mucosa. Strohmeyer (209) thinks he has found a chronic trauma in the pressure caused by the advancing ingesta. He arrived at this conclusion from the well known form of the ulcer, *i.e.*, sloping sides like a funnel, which corresponds to the progressive movements of the stomach contents. He states that the accepted reason for the oblique form of ulcers, namely, the oblique course of the vessels, is not constant, but varies with the degree of filling of the stomach.

An injury with subsequent ulcer can furthermore result from bacterial occlusion of the vessels (Neumann (179)). It has already been mentioned that many authors have accepted the theory of an infectious origin for those following resections of the omentum. Nauwerk (210) and recently Fritz Mayer (211) have given definite proof that bacterial embolism causes a large number of so-called erosions which, since Virchow, have been correctly regarded as forerunners of ulcers. From the literature and from cases of his own, W. Busse (198) concludes that hemorrhagic erosions, particularly those occurring post-operatively result from emboli, whether the latter are infected or not. Actually, many experimentors (212) could obtain ulceration of the gastric mucosa by the intravenous or subcutaneous injection of all sorts and varieties of bacteria. Singer (213) found gastric ulcers in 71 per cent. of rats kept under unhygienic conditions and fed with bread contaminated with their own feces, and Turk (214) found chronic progressive ulcers in dogs which had been fed large amounts of colon bacilli and housed in unfavorable surroundings.

For the development of duodenal ulcer, Moynihan holds a previous appendicitis responsible, accepting, therefore, the theory of an infectious origin. This conception is not ratified by most German surgeons (215).

[There is considerable circumstantial evidence in favor of ulcer following appendicitis in not a few cases. In the surgical clinic of our own hospital, we have had a number of notable examples in which a second laparotomy six months or later after operation for acute appendicitis has revealed ulcer. It is not certain that the ulcer developed subsequent to the appendicitis but careful questioning failed to reveal previous symptoms suggestive of the condition. A long series of experiments on dogs and rabbits led to no conclusive results but other work with india ink (unpublished) showed that lymphatic drainage from the region of the appendix may carry material to the region of the duodenum and pylorus. At any rate, the idea that infection plays an important role in the origin of ulcer cannot be denied and the appendix need not be the source even if it is the commonest site of infection in the abdomen. The tonsils or other foci may be implicated. Rosenow's work, while it can be criticized, is at least very suggestive.]

Naturally, in the cases recorded in pathological anatomical literature as infectious, it cannot be positively determined whether the infection is primary or secondary, since ulcers provide such a suitable pabulum to the bacteria with which they are constantly surrounded.

A case of Breus (216) is especially interesting in this connection. He reports an ulcer resulting from erosion by potash, which became secondarily infected by the tubercle bacillus. In addition to this case, other tuberculous ulcers have been described by various authors (217). Very little is proved by finding such ubiquitous organisms such as staphylococci, streptococci, colon bacilli, mycelia, etc. at the base of an ulcer (see cases of Sjubimowa (218), Rosenow (219), and others) while the presence of specific organisms and also of perhaps specific histological changes such as in anthrax, typhoid, syphilis and especially tuberculosis have a greater value but are by no means convincing. Tuberculous infection is relatively the most frequent of those named, and the portals of entry of this organism are better known (220). Infection may occur from the serosa or through the mucosa or by way of the lymph or blood vessels (221).

It seems probable that in all cases in which infection is the cause of the ulcer, the primary factor must be a defective circulation whether it occurs mechanically by bacterial obstruction or reflexly through spastic contraction of the nutrient vessels.

The theory which seems to hold the center of interest at the present time, although in rejuvenated form, refers to the influence of the nervous system on the formation of ulcer. This was investigated experimentally as early as 1828 by Cammerer (222) who attempted to produce destruction of the stomach wall by resection of the vagus and administration of acetic acid. Talma (223) also speaks of the importance of this nerve. He says

that irritation leads to a contraction of the musculature "which, if prolonged may cause the formation of round ulcers." The experiments of v. Ijzeren (224) are very interesting in this connection. He sectioned the vagus below the diaphragm and among 20 rabbits he found 10 with ulcers, the oldest of which was 28 to 29 days. In addition to regenerative processes there were also "degenerative changes which prevented healing." Lichtenbelt (225) and Antonini (226) found similar ulcers after vagus resection, but other authors had negative results in this respect (227). Clinically, Singer (228) observed a case in which the vagus nerve was surrounded by tuberculous lymph nodes and the symptoms of the patient were like those of duodenal ulcer.

Furthermore, attempts were made to produce gastric ulcers by irritation or destruction of the cœliac ganglion or the sympathetic nerve. Foremost among those to obtain positive results was Della Vedova who found 41 per cent. of ulcers after destruction of the cœliac ganglion, and 60 per cent. after destruction of the splanchnic nerve. Kobogashi (229) and Kawamura (230) also observed multiple erosion in the gastric mucosa, not only after pricking or extirpation of the cœliac ganglion but also after section of the spinal cord, or ligation of the vagus nerve. Schiff (231), Ebstein (232) and others saw such ulcers after section of the optic thalami, cerebral peduncles, medulla oblongata, and spinal cord. In short, there is a large amount of experimental data in the literature which shows that gastric ulcers may be caused by disturbances in the equilibrium of the vegetative nervous system. There is much confusion, however. In many experiments on dogs, Gundelfinger (233) could never produce defects in the stomach or duodenum by procedures on the vagus, but always obtained them by extirpation of the cœliac ganglion. Nagamori (234) could produce them in rabbits by stimulation of the cœliac plexus.

Just as it happens so often in the history of medicine, these findings have been given widely differing interpretations. Klebs (235) esteems the nervous system very highly as the causative factor in ulcers. He was of the opinion that the injury to stomach wall, which is the primary cause of the formation of ulcer, is brought about by vessel spasm, an opinion which Cohnheim (236) and after him many others, have disputed, because they believe such a spasm would not be of sufficient duration. The idea has been recently revived by Beneke (237), is now steadily gaining ground, and today we find it very widely recognized. Internists especially are its supporters, but there are also many among pathological anatomists (238). Thus Rossle (239) actually speaks of ulcers as "secondary diseases," because pathologically anatomically he has usually found with them other preceding changes, especially an old appendicitis, which are said to have brought about the reflex vessel spasm. According to Hart, this applies



principally to the ulcers in older persons where coincident arteriosclerosis exists, and in whom, a *priori*, some sort of pathological process is to be assumed on account of the age. According to Lichterbelt, there are contractions of the muscularis mucosa which can be seen quite plainly with the x-rays (von Bergmann (238)) and which are usually accompanied by cramp-like pains in the abdomen. This pathological contraction is said to result from increased irritability of the vagus. The investigations of Westphal (238) also support this conception. He obtained ulceration of the gastric mucosa by generous doses of pilocarpin and other substances which irritate the vagus. Furthermore, the experience of internists may be cited (Januschke (238)) who by giving atropine, have caused the prompt disappearance of painful colic. Rosler (240) tells of a number of interesting cases of ulcer in lead poisoning. In these, roentgenological contractures of the ring muscle in the form of hour-glass stomach could be demonstrated long before an ulcer appeared, and he concluded that ischæmia from vessel cramp was the immediate cause of the ulcer in these cases.

Since experimental attempts to produce anemia of the mucous membrane by vessel cramp give somewhat irregular results, and especially since in animals it is seldom possible to produce chronic ulcers, as we see them in man, there must doubtless be assumed that a certain constitutional weakness operates in individuals affected by the disease (241). It had always been observed that weakly persons, especially chlorotic girls, are subject to gastric ulcer, and, therefore, particular physical conditions have been considered of much importance. In experimental animals, as has already been mentioned, such physical weakness has been established by caging them in dark, damp places with no opportunity for moving about (Turk and others), or artificial anemia has been produced by bleeding (Quincke and Dettweiler (242)). Following such procedures, ulcers caused by thermic or chemical means healed more slowly. Silbermann (243) and Futterer (244) increased this artificial anemia by pyrogallol, and Litthauer (187) by pyrocin, all with positive results. The gastric lesions healed slowly or not at all. But this also is true of other wounds. They do not heal as well in anemic as in normal individuals. A gastric wound does not become a chronic ulcer just because of anemia. Experiments to produce vessel spasm and thus provoke ulcer formation were made by Licini with adrenalin (245) but the ulcers thus produced healed very quickly.

If it can be shown that there is not only an indefinite "constitutional weakness" in those individuals with ulcers, but an actual predisposition of the vessels in the neighborhood of the stomach to cramp, a factor of importance will have been discovered. This presupposes an increased

irritability of the vegetative nervous system, a condition which in the last few years has been considerably illuminated, especially through the work of Eppinger and Hess (246). Great credit is due these authors for bringing into experimental reach the knowledge of constitutional weakness in the regions supplied by the vagus and sympathetics. They have introduced a "dynamic function test" and have shown that certain individuals respond strongly to atropin and pilocarpin while relatively insensitive to substances stimulating the sympathetic such as adrenalin. The reverse occurs in other individuals.

Supported by these experiments, von Bergmann (247) has sought and found a similar constitutional weakness in the vegetative nervous system of his patients with ulcer. On the basis of later observation, the somewhat too diagrammatic classification of vagotomy and sympathetotomy has been abandoned (248). In most instances, the disturbances occur in both spheres (see Martius (241)) and even if a special nerve is not diseased, it does not exclude the possibility of a weakness in the vegetative system. According to Baur (90) it is a "degenerated soil" on which ulcers form, but it must remain an open question whether there is a lymphatic constitutional anomaly, or an asthenia, in the sense of Stiller (90) or some other form of degeneration. The regional distribution of gastric ulcer (for instance they are seldom observed in Brazil) also points to such factors (racial peculiarity) as well as to the influence of living conditions and nutritional circumstances (249). These findings, described above, furthermore, give us an explanation of why the old stomach remedy, belladonna, gives us good results, and why morphin, which increases spasm and gastric secretion, fails so often in gastric pain.

The spasms chiefly affect the pylorus, although the ulcers are distant from that region, or even when they are in the duodenum. Hunger pain, in duodenal ulcer, does not usually arise on an entirely empty stomach, rather the organ is filled with hyperacid fluid when the pylorus is spastically closed during a hunger pain. If the patient eats, the pylorus opens and the gastric fluid flows out. Probably this hunger pain is only a result of pylorospasm (see Haberer (215)).

The results of Bolton (250) may perhaps be explained as following reflex anemia. He obtained a so-called gastro-toxic serum by the intraperitoneal injection of stomach cells of heterologous species and then injected this serum into the stomach wall of an experimental animal. Deep ulcers resulted but thrombosis did not occur, as his accompanying pictures show. The description of the animal's condition after the injection, greatly resembles that seen in anaphylaxis.

Gundermann (251) thinks the ulcers produced by him, after ligation of branches of the portal vein were due to liver injuries, that is, also of

toxic origin and he does not believe they were due to thrombosis. The injection of liver extract into the ear vein of a rabbit was followed by subserous and submucous hemorrhages into the gastrointestinal tract and in some instances by collapse. Perhaps, as in uremic erosions, it is permissible to assume a reflex ischemia as the course of the ulcers. [All experiments of this nature are open to the objection of what might be called non-specificity. It cannot be too strongly urged that whenever extracts or fluids or other foreign substances are introduced into the body, two possibilities must be considered. When any result is obtained, ask first, is it general, and does it occur with any such substance; ask second, is it specific for the substance in question.]

Krempelhuber (92) believes that anemia of the mucosa can be brought about purely mechanically by the gastropexia which is present in some 88 per cent. of cases of ulcer.

The question now arises what operations can be done for gastric ulcer and how do they affect the disease? Resection of the ulcer bearing area is the easiest to understand. The changes affecting the mechanism and chemistry, following pyloric resection, have been previously discussed. But it cannot be denied that new ulcers may arise in other parts of the stomach after resection (252).

The way in which a *gastroenterostomy promotes healing* is not easy to explain from a physiological standpoint, but that it does is a fact which must be accepted as proved by innumerable clinical observations. This is particularly demonstrable, as Kausch remarks (253) when a calloused ulcer is first treated by gastroenterostomy and then, after four to six weeks, on account of a suspicion of carcinoma, the radical operation is performed. The ulcer is then often found completely or almost healed. This is especially true of ulcers located at the pylorus and in these the end results, according to the study of von Redwitz, are just about as satisfactory as after resection. Other authors (254) believe that ulcers distant from the pylorus can also, in a large majority of cases, be made to heal by gastroenterostomy alone. This view is not universally accepted, although reports of healing after gastroenterostomy of the most severe type of ulcer, distant from the pylorus are plentiful (255). This alone interests us here, since we do not wish to discuss operative methods. In animals, von Izerem (224) found that after section of the vagus, he did not obtain an ulcer, as usual, when he performed a gastroenterostomy at the same time. Since, however, other authors have not consistently observed ulcers, following section of the vagus, care must be observed in the interpretation of this experimental result. Fibich (190) has further studied the healing of gastric ulcers after gastroenterostomy. He produced them by ligation of gastric vessels with excision and cauterization of the

mucous membrane, and they showed no tendency to heal without gastroenterostomy. After this procedure, however, they healed in about three days like ordinary stomach wounds. All these experiments have aroused animated opposition especially since Korte, Clairmont and others, as above recorded, could never produce progressive ulcers under exactly similar experimental circumstances. For this reason, the results of Fibich are probably coincidences, which allow of no conclusive deductions. Clairmont (187) following Fibich, repeated the experiments and came to the conclusion that up until that time (1908, before Payr's work it had not been possible to produce a true gastric ulcer in animals), the healing of defects of the mucosa which occurred in about three weeks in the cardia and in six to seven weeks at the pylorus was not hastened, when a gastroenterostomy was performed at the same time.

In spite of all this, how are we to explain the undoubted healing action of gastroenterostomy? Two factors may be taken into consideration; first, changes in the motor function and second, changes in the chemistry. We have seen that in comparison with the normal stomach the changes in the motor function are only of relatively minor importance. We must not forget, however, that in a large number of the cases operated for ulcer, the pylorus is not completely patulous because of mechanical obstruction either by an ulcer, or by a pylorospasm produced reflexly by an ulcer in another part of the stomach. In both cases, the gastroenterostomy opening operates purely mechanically; it undertakes the emptying of the stomach until the ulcer heals, and the obstruction to the pyloric opening is removed. It has also been observed in ulcers distant from the pylorus that pylorospasm disappears after operation (256). Undoubtedly, this better evacuation of the stomach cannot alone explain the rapid healing because the same injurious factor, digestive action of the gastric juice, is still active after operation. The second factor under consideration is the change in the chemistry (117, 257). Hydrochloric acid is neutralized by the backflow of alkaline intestinal contents and this inhibits its necrosing effect on the cells of the stomach wall. Since the intestinal fluid cannot reach all parts of the stomach, but acts only in the neighborhood of the pylorus, it is easily comprehensible why ulcers in the cardia or on the lesser curvature heal with so much more difficulty than those at the pylorus, and Clairmont (258) has actually pointed out that results of gastroenterostomy in ulcers distant from the pylorus, are much poorer than those in ulcers at the pylorus. For this reason, a large number of surgeons treat the former principally by resection.

When a *gastrostomy* is performed on account of stenosis of the esophagus, all the gastric stimuli from chewing, tasting, etc. disappear. The manner of response of the gastric glands to the sight of food, to chewing



and to tasting, has been established by many experiments and was briefly mentioned before. The process when these are removed has also been studied (259). [In patients with gastrostomy openings, the flow produced by the sight of food can, of course, be preserved although Carlson's observations indicate that the amount is less than would be expected from Pawlow's experiments on dogs. It will probably vary considerably in different individuals. It can also be tasted and chewed by these individuals.] Placing the food immediately in the stomach, however, also leads to secretion and digestion will thus proceed, although there is said to be a diminution of both hydrochloric acid and pepsin (Babkin 33, p. 127). The x-ray studies of Cohn (260) give data regarding the motor activities under these conditions. He found that the usual contrast meal was quickly evacuated, but the addition of oil to the food slowed the emptying rate. The motor function of the stomach is therefore greatly dependent on the sort of food supplied. He could not observe peristalsis of the stomach but systematic studies sufficient to give useful information for the feeding of such patients are lacking.

It might be mentioned in passing that feeding per rectum produces no gastric secretion whatever.

#### LITERATURE TO STOMACH

1. Best, F. and Cohnheim O.: "Zur Roentgenuntersuchung des Verdauungscanals," *Munch. Med. Wchschft.*, 1911, 58, p. 2732-2734.
2. Grodel, F. M. and Seyberth, L.: "Tierexperimentelle Untersuchungen uber den Einfluss der Roentgenmahlzeit auf die Magensform," *Archiv. f. Verdauungs-krankheiten*, Berlin, 1912, 18, p. 8-18.
3. Simmonds, Morris: "Ueber die Form u. Lage des Magens unter normalen u. abnormen Bedingungen," Fischer, Jena, 1907.
4. Petersen, Walther: "Anatomische und chirurgische Beitrage zur Gastroenterostomie," *Brun's Beitr. z. klin. Chirurg.*, 1900, 24, p. 601. Also Simmonds (3). Doyen: "Traitement chir. des affect. des l'estomac et du duodenum," 1895, Paris, Rueff.
5. Jonas, S. and G. Holzknacht: "Die Rontgenuntersuchung des Magens und ihre diagnostischen Ergebnisse," *Ergeb. d. Inn. Med.*, 1909, 4, p. 455.
6. Also Holzknacht and Jonas (5). Groedel, F. M.: "Die Bewegungsvergange am normalen und pathologischen Magen im Lichte der Roentgenstrahlen," *Verhandlungen d. deutsch. Kong. f. innere Med. Wiesb.*, 1912, 29, 91-95; "Die Magenbewegungen," *Erganzungsband zu die Fortschritten auf. d. Gebiete d. Rontgenstrahlen*, 1912, p. 18. Faulhaber: "Die Roentgenuntersuchung des Magens," *Archiv. f. phys. Med. u. med. Techn.*, 1908, 3, 2034, 1909, 4, 3, 3 pl.
7. Wilms (3), also Elze: *Med-naturhistorisches Verein, refer.*, *Munch. Med. Wchschft.*, 1917.
8. Macleod, J. J. R.: *Physiology and biochemistry in mod. med.*, Mosby, St. Louis, 1918, p. 451.
9. Cohnheim, Otto: (23 Vorlesungen fur Studierende und Arzte), *Physiologie d. Verdauung und Ernahrung*, Urban and Schwarzenberg, Berlin, 1908, p. 15.

See also Aschoff, Ludwig: (pamphlet), Ueber d. Engpass d. Magens Fischer, Jena, 1918 (Isthmus ventriculi ein Beitrag zum funktionell-Anatomischen Aufbau des Magens), 63 pp.

10. Hofmeister, Franz: "Über Resorption und Assimilation der Nährstoffe," Archiv. f. exp. Pathol., 1886, 20, p. 291.
11. Kastle, C., Rieder, H., Rosenthal, J.: "Ueber kinematographisch aufgenommene Roentgenogramme (Bio-Roentgenography) der inneren Organ des Menschen," Munch. med. Wchschft., 1909, 56, p. 280.
12. Fleuier, W., for lit.: "Neue Beiträge zur Pathologie des Magens," Munch. med. Wochschft., 1919, No. 22, 579, No. 23, 623, No. 40, 1135, No. 41, 1169.
13. Forssell, Gosta: "Ueber die Beziehungen der Röntgen bilder des menschlichen Magens zu seinem anatomischen Bau," Grafe, Hamburg, 1913.
14. Schwarz, G.: "Versuch eines Systems der physiologischen und pathologischen Magen peristaltik," Fortschritte auf d. Gebiete d. Röntgenstrahlen, 1911, 17, p. 128-141: 1 pl.
15. Müller, Albert: "Wie ändern die von glatter Muskulatur umschlossenen Hohlorgane ihre Grösse?" Arch. f. Physiol., 1907, 116, 252.
16. Kastle, Rieder and Rosenthal: Ztschrft f. Röntgenkunde, 1910-1911, 12.
17. Holzknecht, G. and Luger, A.: "Zur Pathologie und Diagnostik des Gastrosasmus," Mitt. aus d. Grenzgebieten, 1913, 26, 669.
18. Brauning, H.: "Die Entfaltung des Magens," "Untersuchungen mit Roentgenstrahlen," Munch. Med. Wochschft., 1909, 56, 277.
19. Cohnheim, Otto: "Beobachtungen ueber Magenverdauung," Munch. Med. Woch., 1907, 52, 2581.
20. Kastle: Fortschritte auf dem Gebiete d. Röntgenstrahlen, 1919, 26.
21. Schuller: "Klinische und experimentelle Untersuchungen ueber die Function des Magens nach Gastroenterostomie und Pylorus resection," Mitt. aus d. Grenzgebieten, 1911, 22, 764.
22. Grutznher, P.: "Ein Beitrag zur Mechanismus der Magenverdauung," Pflügers Arch., 1905, 106, 463. Ellenberger: "Zum Mechanismus der Magenverdauung," Pflüger's Arch., 1906, 114, 93.
23. Canon, W. B.: (1) "Movements of stomach studied by Röntgen Rays," (2) "Passage of food-stuffs from the stomach," Am. Journ. Physiol., (1) 1898, 1, 359; 2, 1904, 12, 387.
24. Duccchesi, Virgilio: See Luciani, Human Physiology, trans. by F. Welby, Macmillan, 1913, p. 192, etc. Vol. II.
25. Pawlow and Boldireff, V. N.: "Passage into the Stomach of a natural mixture of pancreatic and intestinal juices; conditions and probable importance of this phenomenon. Translation," Zentralbl. f. Physiol., 1904, 18, 489.
26. Egau, E.: "Ueber das Schicksal und die Wirkung heisser und kalter Getränke im Magen," Munch. Med. Woch., 63, 1916, 2, 37-40.
27. Tobler, L.: "Ueber die Eiweissverdauung im Magen," Ztschrft f. phys. Chem., Strassburg, 1905, 45, 185-215.
28. V. Mering and Aldehoff: 12 Kongress f. innere Med., 1893, 471. Moritz: "Studien ueber die Motorische Thatigkeit des Magens," Ztschrft. f. Biol., 1901, 42, 565. Hirsch: Zentralblatt f. inn. Med., 1901, 33, 1892, 993; 1893, 73, 377, 601.
29. Otto, E.: "Ueber das Verhalten von Salzlosungen in Magen," Arch. f. exp. Path. u. Pharmacol., 1905, 52, 370.
30. Müller, Johannes: Ztschrft. f. diat. Therapie 8, Hft. 2.
31. For literature on control of pylorus see: Wheelon H. and Thomas, J. E.: "Rhythmicity of the pyloric sphincter," Am. J. Physiol., 1920, 54, 460. Luckhardt,

- A. B., Phillips, H. T., and Carlson, A. J.: "The control of the pylorus," *Am. J. Physiol.*, 1919, 50-57.
32. Editorial: *J. A. M. A.*, 1921, 76, 729.
  33. Babkin, B. P. for lit.: "Die aussere Sekretion der Verdauungsdrusen," Berlin Springers Verlag, 1914, 407 pp.
  34. Abderhalden, Emil: *Physiol. Chemie*, 1909, 661. Berlin, Urban.
  35. Pawlow, Ivan P.: Transl. into English by W. H. Thompson, London, Griffin, 1902. "Die Arbeit der Verdauungsdrusen, Deutsch von A. Walther, Bergmann, Wiesbaden, 1898.
  36. Cohnheim and Marchand: *Ztschr. f. Physiol. Chemie.*, 1909, 63, 41.
  37. Edkins, J. S.: "The chemical mechanism of gastric secretion," *Journ. of Physiol.*, 1906, 34, 133. Gross, Walter: "Beitrag zur Kenntniss der Sekretionsbedingungen des Magens nach Versuchen am Hund," *Arch. f. Verdauungskrankheiten*, 1906, 12, 507.
  38. Popielski: *Zentralbl. f. Physiol.*, 1902, 16, 121.
  39. Schiff and Contejean: *Contrib. a. l'etude de la physiol. de l'estomac*, These de Paris, 1892.
  40. Bogen, H.: "Experimentelle Untersuchungen ueber psychische u. assoziative Magensaft secretion beim menschen," *Pflugers Archiv.*, 1907, 117, 150. Bier-nacki, E.: "Die Bedeutung der Mundverdauung und des Mundspeichels fur die Thatigkeit des gesunden und kranken Magens," *Ztschrft. f. klin. Medizin.*, 1892, 21, 97. Umber: "Die Magensaftsekretion des (gastroenterostomie) Menschen bei Scheinfuttening und Rectalernahrung," *Berliner klin. Wochen-schrift*, 1905, 52, 56-60. Hornborg, A. F.: "Beitrage zur Kenntniss der Absonderungs bedingungen des Magensaftes beim Menschen," *Skand. Arch. f. Physiol.*, Leipzig., 1904, 15; 209. Bickel, A.: (1) "Experimentelle Unters-uchungen uber den Einfluss von Affekten auf die Magensaftsekretion," *Leipzig. u. Berl.*, 1905, 31, 1829; (2) "Experimentelle Untersuchungen ueber Magensaft-sekretion beim Menschen," *Deutsche Med. Wochenschrift*, 1906-1907, 32, 1323.
  41. Tschekunow, J. S. (et al): "Weitere Untersuchungen uber die Verdauung Resorp-tion under normalen und pathologischen Verhaltnissen," *Ztschrft. f. Physiol. Chemie.*, 1913, 87; 316.
  42. Uffenheimer, A.: "Physiologie des Magen-Darmkanales beim Saugling und alteren Kind," *Ergebn. f. innere Med.*, 1908, 2, 271.
  43. Langley, J. N.: "Das sympathische u. verwandte nervose Systeme d. Wirbel-tiere," *Ergebn. d. Physiol.*, 1903, 2, 830.
  44. Openchowski, A. G.: "Physiologischen Gesellschaft uber lentren und Leitungs-bahnen fur die Musculatur des Magens," *Arch. f. Anat. u. Physiol.*, 1889, June, p. 549.
  45. Magnus, R.: "Die Bewegungen des Verdauungskanales," *Ergebn. d. Physiol.*, 1907, 7, 28. Magnus, R.: (4) "Versuche am uberlebenden Dunn darm von Säugetieren," *Pflugers Arch.*, 1906, 111, 152; (3) "Versuche am uberlebenden Dunn darm von Säugetieren," *Pflugers Arch.*, 1905, 108, 1; (1) "Versuche am uberlebenden Dunn darm von Säugetieren," *Pflugers Arch.*, 1904, 102, 123, and 349, Part 1; (2) "Versuche am uberlebenden Dunn darm von Säugetieren," *Pflugers Arch.*, 1904, 103, 515, and 525, Part 2.
  46. Pawlow, J. P. and Schumow-Simanowskaja: "Beitrage zur Physiologie der Absonderungen Die Innervation der Magendrusen beim Hunde," *Arch. f. Anat. u. Physiol.*, 1895, p. 53-65.
  47. Bayliss, W. M. and Starling, E. H.: "The movements and the innervation of the large intestine," *J. Physiol.*, 1900, 26-107.

48. Elliot, T. R. and Smith, E. B.: "On the innervation of the ileocolic sphincter," *J. Physiol.*, 1904, 31, 157-168.
49. Popielski, L.: "Zur Physiologie des Plexus coeliacus (experimentelle Untersuchungen)," *Archiv. f. Anat. u. Physiol.*, 1903, 338.
50. Goltz, F., Goltz and Ewald: (1) "Über die Functionen des Lendenmarks des Hundes," *Pflüger's Archiv.*, (1) 1874, 8, 460; (2) 1896, 63, 362.
51. Frankl-Hochwart, L. and Fröhlich, A.: "Über Tonus und Innervation der Sphinkteren des Anus," *Pflüger's Archiv.*, 1900, 81, 420.
52. Courtade, D. and Guyon, J. F.: "Pneumogastrique," *Journ. de Physiol.*, 1899, 1, 348.
53. Exner, Alfred: "Wie Schützt sich der Verdauungstract vor Verletzungen durch spitze Fremdkörper?" *Pflüger's Archiv.*, 1902, 89, 253.
54. Muller, L. R.: "Beiträge zur Anatomie, Histologie und Physiologie des nervus vagus, zugleich ein Beitrag zur Neurologie des Herzens, der Bronchien, und des Magens," *Deutsch. Archiv. f. klin. Med.*, 1910, 101, p. 421. Kirschner, M. and Mangold, E.: "Die motorische Funktion des Sphincters pylori und des Antrum pylori beim Hunde nach der queren Durchtrennung des Magens," *Mitt. aus d. Grenzgebieten*, 1911, 23, 446-494. Klee, P.: "Die Magenform bei gesteigertem Vagus und Sympathikustonus," *Munchener med. Wochenschrift*, 1914, 61, 1044-1047.
55. May, W. P.: (1) "The movements and innervation of the stomach," *Brit. Med. Journ.*, 1902, 2, 779, 895; (2) "The innervation of the sphincters and musculature of the stomach," *J. Physiol.*, 1904, 31, 260-271.
56. Cannon: *Zentralbl. f. Physiol.*, 1906, 20, 613. Cannon, W. B.: "Motor activities of the stomach and small intestine after splanchnic and vagus Section," *Am. J. Physiol.*, 1906, 17-429.
57. Dr. Van Braum-Honckgeest: "Untersuchungen ueber Peristaltik des Magens und Darmkanals," *Pflügers Archiv.*, 1872, 6, 266.
58. Cited by Magnus: (2) "V. Duccesi," "Sulle funzioni Motricidello stomacho," *Archiv. per le sc. med.*, 1897, 21, No. 5; (1) *Ergebnisse d. Physiol.*, 1908, 3, 38.
59. Klee, R.: "Beiträge zur pathologischen Physiologie der Mageninnervation," 1. Mitteilung: Der Brechreflex, *Deut. Archiv. f. klin. Med.*, 1919, 128, 204.
60. Exner, A. and Jaeger: "Zur Kenntniss der Funktion des Ganglion Coeliacum," *Mitt. aus d. Grenzgeb.*, 1909, 20, 645.
61. Alvarez: "The motor functions of the intestine from a new point of view," *J.A.M.A.*, 1915, 65, 388.
62. V. Brun, (K. O.), Max: *Die Allgemein Narkose*, Stuttgart, Enke, 1913. (In—Von Bruns, P. Editor, *Neue Deutsch Chirurg.*, Vol. 5, 1913.
63. Forster, O. and Kuttner, H.: "Ueber operative Behandlung gastrischer Krisen durch Resection der 7-10 hinteren Dorsalwurzel," *Brun's Beiträge z. klin. Chirurg.*, 1909, 63, 245-256.
64. Lennander, K. G.: "Über Hofrot Nothnagels zweite Hypothese der Darmkolikschmerzen," *Mitt. aus d. Grenzgeb.*, 1906, 16, 19.
65. Muller, A.: "Der Einfluss der Salzsäure auf die Pepsinverdauung," *Mitt. aus d. Grenzgebieten*, 1908, 18, Hft. 4. *Deutsches Archiv. f. klin. Med.* Leipzig, 1908, 94, 27-45.
66. Talma, S.: "Zur Behandlung von Magen," *Ztschft. f. klin. Med.*, 1884, 8, 407.
67. Schmidt, J. E.: "Ein Beitrag zur Frage der Magensensibilität," *Mitt. aus d. Grenzgebiet*, 1908, 1909, 19, 278.
68. Carlson: "The origin of the epigastric pains in gastric duodenal ulcer," *Am. J. Physiol.*, 1907, 45-81.



69. For discussion and lit. see Carlson, A. J.: "On the nervous control of the hunger mechanism," Harvey lectures 1915-16, 137, Lippincotts.
70. Rheinboldt, M.: *Int. Beitr. z. Pathol. u. Therapie d. Ernährungsstörungen*, 1910, Vol. 1, 1.
71. Fritsch, K.: "Das Ulcus ventriculi perforans als Etiologie der Pancreas necrosa," 1910, *Beitr. z. klin. Chir.* Tübing., 1910, 66, 101-112, *Bruns Beiträge z. klin. Chir.*, 1910, 70, 559. Katschkowsky, P.: "Das Weberlebender Hunde nach einer gleichzeitigen doppelten Vagotomie am Halse," *Pflügers Archiv.*, 1901, 84, 6.
72. Exner, A., Schwarzmann: "Ein neues Operations verfahren tabetischer crises gastriques," *Mitt. aus. d. Grenzgebieten*, 1914, 28, 31. *Deutsche Zeitschr. f. Chir.* v. 111, p. 576, 1911. Exner, A.: "Ein neues Operations verfahren. tabetschen crises gastriques." *Deutsche Zeitschr. f. Chir.*, 1911, 111, 576-590
73. Krehl, Ludolf: "Über die Folgen der Vagusdurchschneidung," *Archiv. f. Anat. u. Physiol.*, 1892, suppl., p. 278.
74. Ibrahim: "Die Pylorusstenose der Säuglinge," *Die Erkennung u. interne Behandlung der hypertrophischen (spastischen) Pylorusstenose der Säuglinge Therap.* *Monatsh. Berl.*, 1908, 22, 560-571; *Ergeb. d. inner. Med.*, 1908, 1, 208.
75. Wilms: "Die Rammstedtsche Operation beim hypertrophischen Pylorospasmus (Dauer-pylorospasmus) der Säuglinge," *Deutsche Ztschft. f. Chir.*, 1918, 144, 63-82.
76. Manasse: *Berliner klin. Wochschft.*, 1917, 255.
77. Brauns, Tuffiers, Payers, A.: "Die postnarkotische Magenlaehmung," *Mitt. aus. d. Grenzgebieten*, 1910, 22, 446.
78. Kelling, Georg.: "Ueber den Mechanismus der acuten Magendilatation," *Archiv. f. klin. Chirurgie*, 1901, 64, 393.
79. Braun, W. and Seidel, H.: "Klinisch-experimentelle Untersuchungen zur Frage der akuten Magenerweiterung," *Mitt. d. Grenzgeb.*, 1907, 17, 533.
80. Kuru, H.: "Ueber die akute Magenerweiterung (Mit. Bemerkungen von B. Naunyn)," *Mitt. aus. d. Grenzgebieten*, 1911, 23, 169-190.
81. Mangold, E.: "Die Lahmung des Magens durch die Inhalationsnarkose," *Munchener med. Wochenschrft.*, 1911, 58, 1861, 1863.
82. Korte: Discussion by Korte in "Freie Vereinigung der Chirurgen Berlin," *Zentralbl. f. Chir.*, 1909, 36, 160.
83. Bier: discussion by Bier in "Freie Vereinigung der Chirurgen Berlin," *Zentralbl. f. Chir.*, 1909, 36, 160.
84. Haberer, H.: "Der arterio-mesenteriale Duodenalverschluss," *Ergebn. d. Chirurg.*, 1913, 5, 475.
85. Cannons, W. B., Murphy, F. T.: "The movements of the stomach and intestines in some surgical conditions," *Ann. Surg., Phila.*, 1906, 43, 512-536.
86. Albrecht, P. A.: "Ueber arterio-mesenterialen Darmverschluss an der Duodeno-Jejunalgrenze und seine ursachliche Beziehung zur Magenerweiterung," *Virch. Archiv.*, 1899, 156, 305.
87. Muller, P.: "Ueber acute post-operative Magendilatation hervorgerufen durch arteriomesenteriale Duodenal compression," *Deutsche Ztschift. f. Chir.*, 1900, 56, 500.
88. Mathieu, A. and Roux, I. C.: "Die klinischen Erscheinungsformen der motorischen Insuffizienz des Magens," *Ergebn. d. inneren. Med.*, 1910, 5, 252-279. Hayem: Cited by Mathieu and Roux.
89. Glenard, Frantz: *Les ptoses viscerales*, Paris, Alcan, 1899.

90. Stillers: "Die asthenische Konstitutionskrankheit" Springers Verlag, 1917. Bauer, Julius: Konst. Disp. zu inn. Krankheiten, J. Springers Verlag, 1917, 398, 586, p. 8.
91. Kussmaul: V. Volkmanns Sammlung. kl. Vorträge, 1880, 181.
92. Krempelhuber, M.: "Zur Pathogenese des runden Magengeschwurs," Deutsche med. Wochenschrift, 1919, 40, 1099.
93. Rovsing, Niels, Thorkied: Translated from Danish by Georg Saxinger "Unterleibschirurgie," Verl. v. F. C. W. Vogel, Leipzig, 1912, p. 194 ff.
94. Reichmann, M.: "Ein Fall von krankhaft gesteigerter Absonderung des Magensaftes," Berliner klin. Wochenschrift., 1882, 40, 606.
95. See No. 88.
96. Marchand: "Prozess d. Wundheilung," Deutsche Chirurg., 1901, 16, 300.
97. Matthes, M.: "Untersuchungen über die Pathogenese des Ulcus rotundum ventriculi und über den Einfluss von Verdauungsenzym auf lebendes und todes Gewebe," Zieglers Beitr., 1893, 13, 308.
98. Graser, E.: "Untersuchungen ueber die feineren Vorgänge bei Verwachsung peritonealer Blätter," Deutsche Ztschrift. f. Chir., 1888, 27, 533. Graser: Arch. f. klin. Chir., 1898, 50.
99. Wilkie, D. P. D.: "Gastro-jejunal and jejunal ulceration following gastroenterostomy," Edinb. med. journ., 1910, n. s. v., 316, 327, 3 pl.
100. Sonnenburg, case of Schroeter, F.: "Ueber Gastroenterostomie," Deutsche Ztschrift. f. Chir., 1894, 38, 305.
101. Chlumsky, U.: "Experimentelle Untersuchungen über die Verschiedenen Methoden der Darmereinigung," Bruns Beiträge, 1900, 25, 539.
102. Perrier and Hartmann Monprofit: Chirurgie de l'estomac, Paris, 1900, Le Gastroenterostomie, Paris, 1903.
103. Kelling, Georg.: "Studien zur Chirurgie des Magens," I Archiv. f. Klin. Chirurgie, 1900, 62, 1. Hesse: "Roentgenologischer Beitrag zur Physiologie und Pathologie des Magen-Darm. Traktus," Verhandlungen d. deutsch. Kong. f. innere Med. Wiesb., 1912, 29, 311-314. Zeitschrift. f. Röntgenkunde, 1912, 14. Schuller: "Klinische und experimentelle Untersuchungen ueber die Function des Magens nach Gastroenterostomie und Pylorus resection," Mitt. aus d. Grenzgebieten, 1911, 22, 715.
104. Seringer: Chir. Kongresszentralbl., 1914, 5, 591.
105. Herre: Zeitschr. f. Röntgenkunde, 1912, 14.
106. Neuhaus, v. Volkmanns Sammlung klin. Vorträge, No. 486.
107. Kocher: Chirurgenkongress, 1902.
108. Schoemaker, T.: "Ueber die motorische Funktion des Magens," Mitt. a.d. Grenzgebieten 1910, v. 21, 30, p. 719-728.
109. Borszeky: "Die chirurgische Behandlung des peptischen Magen und Duodenalgeschwure und seiner Komplikationen und die damit erreichten end Resultati," Bruns Beiträge z. klin. Chir., 1908, 57, 172.
110. Cannon, W. B. and Blake, J. B.: "Gastroenterostomy and pyloroplasty; an experimental study by means of the Rontgen rays," Ann. of Surgery (Phila.), 1905, 41, 686-711.
111. Leggett, N. B. and Maury, J. W. D.: "Studies upon the function of the pylorus and stoma after gastroenterostomy has been performed," Ann. of Surgery, 1907, 46, 549.
112. Kuttner, Herman: "Beiträge zur Chirurgie des Magens auf Grund von 1100 in Jahren behandelten Fällen (Aus der Chirurgischen Klinik in Breslau)" Arch. f. klin. Chir., 105, 797.

113. Barsony, Theodor.: "Aus der Chirurgischen Klinik zu Budapest," *Bruns Beitr. z. klin. Chir.*, 1913, 88, p. 473.
114. Wettstein, A.: "Zur Chirurgie des Magens und des Duodenums," *Sammelreferat Wettstein, Med. Kl.*, 1915, 11, 950, 976.
115. Hartman, H. and Soupault, M.: "Les resultats eloignes de la gastro-enterostomie," *Revue de Chirurgie*, 1899, 14, p. 137. Schlesinger, E.: "Ueber Gastro-Pyloro-Duodenoptose als Ursache des Einfließens von Darmsaft, Galle und Pancreassaft in den Magen," *Zeitschrift. f. klin. Med.*, 1912, 75, p. 314. Kausch, W.: "ueber funktionelle Ergebnisse nach Operation am Magen bei gutartigen Erkrankung," *Mitt. a.d. Grenzgebieten*, 1898, 4, 347.
116. Krause, Fedor: "Erfahrungen in der Magen Chirurgie," *Berliner kl. Wochenschrift*, 1903, No. 47, p. 1070.
117. Katzenstein: "Ueber Aenderung magen Chemismus nach der Gastroenterostomie und den Einfluss dieser Operation auf Ulcus u. Carcinoma," *Deutsche Med. Wochenschr.*, 1907, 33-95.
118. Kausch and Kaplan: *Zeitschrift. f. physiol. Chemie*, 1913, 87, p. 338.
119. Abderhalten, Emil: *Lehrbuch d. physiol. Chemie*, 2 Aufl., 1906, p. 282, Berlin, Urban.
120. Heinsheimer, F.: "Stoffwechseluntersuchungen bei zwei Fallen von Gastroenterostomie," *Mitt. a.d. Grenzgebieten*, 1896, 1, 348.
121. Dagaew, W. F.: "Aenderungen in den Verdauungsprozessen nach Gastroduodenostomie und Gastrojejunostomie und nach total Magen extirpation," *"Mitt. a.d. Grenzgebieten"*, 1913, 26, page 183.
122. Bayliss, W. M., Starling, E. H.: (1) "Mechanism of pancreatic secretion," (2) "Uniformity of Pancreatic mechanism in Vertebrata," *Journ. of Physiol.*, 1902, 28, p. 325; 1903, 29, p. 174.
123. c.f. Cohnheim, O. and Klee, P.: *Zur Physiologie des Pancreas Ztschr. f. physiol. Chem. Strassb.* 1912, 78, 464-484, *Zur Physiol. d. Pancreas, Heidelberg. Akad. d. Wissenschaft, mathnaturwissensch. Klasse*, 1912, 3.
124. Bickel, A.: "Beobachtungen an Hunden mit extirpiertem Duodenum," *Berliner klin. Wochenschrift*, 1909, 46, 1201.
125. Rost, F.: "Die funktionelle Bedeutung der Gallenblase. Experimentelle und anatomische Untersuchungen nach Cholecystectomy," *Mitt. a.d. Grenzgebieten*, 1913, 26, 710.
126. Kelling: "Ein in physiologischer werther Fall von Magen resection nebst Bemerkungen zur Gastroenterostomie," *Deutsche Zeitschr. f. Chir.*, 1901, 60. S. 155.
127. Casagli, F.: "Modificazioni della parete del duodeno in sequito alla gastroenterostomia, studio sperimentale," *Firenze L. Niccolai*, 1913, p. 173, 3 pl. 8th Chir. Kongresszentralbl. 4, p. 446.
128. Chlumsky, V.: (1) "Ueber die Gastroenterostomie," (2) "Uber die Gastroenterostomie," *Bruns Beitrage*, 1898, 20. 2312, 487. 1900, 27, 311, lit.
129. Dastre quoted by Tavel, E.: "Reflux dans la gastro enterostomie," cited by Tavel, *Revue de chir.*, 1901, 2, 690.
130. Dr. Steudel: "Die in den letzten Jahren an der Czernyschen Klinik ausgefuhrten Magenoperationen und die Endresultate der fruheren Operationen," *Bruns Beitr. z. klin. Chirurgie*, 1899, 23, S. 387.
131. Kelling, Georg.: "Studien zur Chirurgie des Magens," 5 *Arch. f. klin. Chirurgie*, 1900, 62, 307.
132. Stuber: "Experimentelle Begrundung der Aetiologie des Ulcus ventriculi," *Deutsche med. Wohnschr. Leipzig and Berl.*, 1914, 40, 987; *ibid.* 1936,

- "Experimentelles Ulcus ventriculi Zugleich eine neue Theorie seiner Genese,"  
Zeitschr. f. exp. Path. u. Therapie, 1914, 16 and Munchner med. Wochenschr.,  
1914.
133. Mathiew and Roger: Inneres Kongresszentralbl. 8, 571.
  134. Wolfier, A.: "Gastro-Enterostomie," Zentralbl. f. Chirurgie, 1881, No. 45, page  
705.
  135. Tavel, E.: "Reflux dans la gastro-enterostomie" (see No. 129), Revue de Chir-  
urgie, 1901, 2, 686.
  136. Bruns, P. et al. Editors: Walter G Kausch im Handbuch d. prakt. Chirurgie,  
1913, 3, 145.
  137. Rockwitz, C.: "Die Gastroenterostomie an der Strassburger Chirurgischen  
Klinik," Deutsche Zeitschr. f. Chirurgie, 1889, 25, 502. Doyen: No. 128.  
cited by Chlumsky in Bruns Beitrage, 1898, 20, 259.
  138. Anschutz, W.: "Ueber die Darmstorungen nach Magen operationen," Mitt. a.d.  
Grenzgebieten, 1905, 15, 305.
  139. Boas, I.: "Ueber gastrogene Diarrhea by Pylorusstenosen," Berlin Klin. Wochen-  
schr., 1912, 49, 337-339.
  140. Hertz, Arthur, F.: "Cause and treatment of certain unfavorable after effects of  
gastroenterostomy," Ann. Surgery, 1913, 58, 466.
  141. Mathiew, A. and Tavignac, R.: "Etude sur les troubles intestinaux consecutifs  
a la gastroenterostomie," Arch. des malad. de l'appar. dig. et de la nutr., 1913,  
541.
  142. Van Roojen, P. H.: "Ueber das Ulcus pepticum jejuni nach Gastroenterostomie,"  
Arch. f. Kl. Chir. Berl., 1909, 91, 381-448; Archiv. f. Klin. Chirurgie, 1910, 91,  
423.
  143. Gosset, A.: "L'ulcère peptique du jejunum apres gastroenterostomie," Revue  
de chirurgie, 1906, 33, p. 54, 290.
  144. v. Haberer, H.: "Ulcus duodeni und postoperationes peptisches Jejunalgeschwur,"  
Arch. f. klin. Chir. Berl., 1918, 109, 413-566; Arch. f. Klin. Chir. v. 101 and  
109; Wiener Klin. Wochenschrift, 1918 and 1919.
  145. Katzenstein: "Der Schutz des Magens gegen die Selbstverdauung nebst einem  
Vorschlag zur Behandlung des Ulcus ventriculi," Berlin. Klin. Wochenschr.,  
1908, 45, 1749.
  146. Kathe, H.: "Zur Frage der Verdauung lebenden Gewebes," Berlin. klin. Wochen-  
schr., N: 1908, 48, 2135-2137, 1911 or 12.
  147. Hotz, G.: "Versuche uiber die Selbstverdauung des Darmes in Magen," Mitt.  
a.d. Grenzgebieten, 1909, 21, 143-153.
  148. Tietze, Alen.: "Experimentelle Untersuchungen uiber Netzplastik," Bruns Bei-  
trage, 1900, 25, 411.
  149. Matthes, M.: (See No. 97) Zieglers Beitrage, v. 13.
  150. Patron: "Ulcus jejuni nach Gastroenterostomie," cited by Exalto, Mitt. aus  
d. Grenzgebieten, 1911, 23, 15.
  151. Braun, Heinrich: "Uber Gastro-Enterostomie und gleich, zeitig ausgefuhrte  
Entero-Anastomose," Arch. f. klin. Chir., 1898, 57, 1892, and 1893, 41, 1893,  
45, 2, 361.
  152. Mayo, Wm. J.: "Gastrojejunal ulcers (pseudojejunal ulcers)," Sur., Gyn. and  
Obstetrics, 1910, X 227-229, 1 pl.
  153. Dagaew, W. F.: "Aenderungen in den Verdauungopprozessen nach Gastroduo-  
denostomie und Gastrojejunostomie und nach totaler Magenexstirpation,"  
Mitt. a.d. Grenzgebieten, 1913, 26, 176. Kaplan, S.: "Digestive processes  
under defects in the region of the stomach, experimental investigation,"



- S. Petersburg, 1913, F. Vaisberg and P. Gershunim, 169, P. 6 tab. 8, Zeitschrift, für physiol. Chemie, 1913, 87, 337. Mering, N.: 15, Kongress f. innere Med., 1897, 433. Schuller, L.: "Klinische und experimentelle Untersuchungen ueber die Funktion des Magens nach Gastroenterostomie und Pylorus resection," Mitt. a. d. Grenzgebieten, 1911, 22, 742.
154. Gocke, C.: "Beitrage zur Morphologie des Magens nach Resektionen," Bruns Beitrage, 1916, 99, 294.
155. Schuller, L.: "Klinische und experimentelle Untersuchungen ueber die Function des Magens nach Gastroenterostomie und Pylorus resection," Mitt. a.d. Grenzgebieten, 1910-11, 22, 1912 or 1911, 742.
156. Redwitz, v.: "Die Physiologie des Magens nach Resection aus der Continuitat Eine experimentelle Untersuchung," Mitt. a.d. Grenzgebieten, 1917, 29, 531-620, 1 pl.
157. Faulhaber, M. and v. Redwitz, E. F.: "Ueber den Einfluss der "circularen Magensection" auf die Sekretion und Motilitat des Magens," Med. Klinik, 1914, X 680-684. Hartel, F.: "Diagnostische und therapeutische Erfahrungen beim Sanduhrmagen," Arch. f. klin. Chirurg., 1911, 96, 1-56. Kummell: Naturforscherversammlung, Wien, 1913. Perthes, G.: "Ueber die Resection des Magens bei Magengeschwur," Arch. f. klin. Chir. 1914, 105, 80-89. Chirurgenkongress, 1914. Stierlin, E.: "Roentgenologische Erfahrungen ueber Magenspasmen," Munchener Med. Wochenschrift, 1912, 59, 796-873.
158. Thoma, E. (L. R. Muller): "Eine Studie ueber die Hungerempfindung," Inaug.-Diss., Wurzburg, 1915.
159. Trinkler, N.: "Zur Frage der totalen Exstirpation des Magens," Arch. f. klin. Chir., 1911, 96, 536. Flechtenmacher: "Ein Fall von totaler Magenextirpation," Deutsche Zeitschr. f. Chirurgie, 1917, 141, 398-408. Grohi, B.: "Die totale Magenentirpation bei Thieren," Arch. f. exp. Path. Pharmacol., 1903, 49, 114. Ito, H. and Asahara, S.: "Beitrag zur totalen resp. sub-totalen Exstirpation des carcinomatosen Magens," Deutsche Zeitschrift. f. Chir., 1905, 80, 135-149. Lit. s. Sasse, F.: "Ulcus callosum ventriculi totale, Extirpation, nebst Bemerkungen ueber den dauernden Verlust des Magens sowie ueber die Technik der Magenresection," Munchen med. Wchnschr, 1913, 60, 650, Zentralbl. f. Chir., 1913. Trinkler, N.: "On complete removal of the Stomach," Khirurgia Mosk, 1911, 39, 437-451, 1 pl., Arch. f. klin. Chir., 1911, v. 96.
160. Kaiser, F. F.: "Beitrage zur den Operativen am Magen," Czerny v. Beitrage zur operativen Chirurgie, 1878.
161. Monari, Umberto: "Experimentelle Untersuchungen ueber die Abtragung des Magens und des Dunndarms beim Hunde," Bruns Beitrage z. klin. Chirurgie, 1896, 16, 479.
162. de Filippi, F.: "Untersuchungen ueber den Stoffwechsel des Hundes nach Magenextirpation und nach resection eines grossen Theils des Dunndarms," Deutsche Med. Wochenschrift, 1894, p. 780.
163. Cohn, M.: "Roentgenuntersuchung einer Frau, welcher der Magen und beide Nervi vagi reseziert worden sind," Berlin klin. Wochenschr., 1913, 2, 1303, Berlin klin. Wochenschr., 1913, 1393-95.
164. Unger, E.: "Operationen am Brusttheil der Speiserohre," Berliner klin. Wochenschr., 1913, 1 (Discussion) 1536, Zentralbl. f. Chir., 1913.
165. Ogata, M.: "Ueber die Verdauung nach der Ausschaltung des Magens," Archiv. f. (Anat. a.) Physiol., 1883, 89.
166. Schlatter, C.: "Ueber Ernahrung und Verdauung nach Vollstandiger Entfernung

- des Magens. Oesophagoenterostomie, beim Menschen," Bruns Beiträge, 1897, 19, 757.
167. Abderhalden, Emil: Lehrbuch d. physiol. Chemi, 1909, 2. ed., p. 282, Berlin, Urban, 1906.
168. Wroblewski: Zentralbl. f. Physiol., 1897, v. 11. Hofmann, A.: "Stoffwechseluntersuchungen nach totalen Magenresektion," Münchener med. Wochenschr., 1898, 18, 560.
169. Ssolovojeff: Diss. St. Petersburg, Ref. Chir. Kongresszentralbl., 1911, 2, 719.
170. Schuchardt, Prof. Dr.: "Ueber Regeneration des Magens nach totaler Resektion," Arch. f. Klin. Chir., 1898, 57, 454.
171. Rouse, J. C. and Riva, A.: "Sur la non digestibilité du mucus intestinal," Compt. rend. Soc. Biol. Par., 1906, 60, 537.
172. de Klug: "Pourquoi les ferments proteolytiques nedigerent-ils pas l'estomac et l'intestin sur le vivant," Arch. int. de physiol., 1907, 5, 297-317, Liege and Par.
173. Danilewsky, cited by Moller, S.: "Die Nichtverdauung der intakten Magenschleimhaut durch den Magensaft," Ergebn. d. inn. Med., 1911, 7, 533.
174. Kaufmann: Arch. d. Verdauungskrankheiten, 1906, v. 12.
175. Edinger, L.: "Über die Reaction der lebenden Magenschleimhaut," Pflügers Archiv., 1882, 24, 247.
176. Hunter: Philosophical Transactions, 1772, p. 450.
177. Bernard, Claude: Paris, Baillière Leçons de physiol. experiment, 1859.
178. Matthes: (See No. 49) Zieglers Beiträge, 1893, 13, 309.
179. Neumann, E.: "Über peptische Magengeschwüre, post mortale und pseudovitale autodigestion," Virchows Archiv. f. Path. Anat., 1906, 184, 383, 360-403.
180. Kehr, J. K.: "Über die Ursache des runden Magengeschwüres," Mitt. a.d. Grenzgebieten, 1914, 27, 679.
181. Virchow: Virchows Archiv., 1853, v. 5.
182. Krasnogorski: (Leipzig, 1913, F. C. W. Vogel) Lit. Antipepsin, Oppenheimer. d. Fermente, 4 edit. 1913, 545, Carl Oppenheimer Die Fermente und ihre Wirkungen.
183. Katzenstein, M.: "Der Schutz des Magens gegen die Selbstverdauung nebst einem Vorschlag zur Behandlung des Ulcus ventriculi," Berlin. klin. Wochenschrift, 1908, 45, 1749-1753. Arch. f. klin. Chir., 100, 4, u. 101, 1, Chirurgen kongress, 1911. Kawamura, K.: "Zur Frage der Verdauung lebenden Gewebes im Magen zugleich ein Beitrag zur Pathogenese des runden Magengeschwüres," Mitt. a. d. Grenzgebieten, 1913, 26, 379-390.
184. Gaspardi, Viola et: "Sur l'autodigestion d l'estomac," Arch. ital. de Biol., 1889, 13, Kongressbericht, 7. Contejean: cited by Moller, l.c. 532.
186. Best: "Zur Frage der Selbstverdauung lebenden Gewebes," Beiträge z. path. Anat. u. z. allg. Path., Jena, 1914, 60, 170-184. Zieglers Beiträge, 1914, 60. Hotz, G.: "Versuche über die Selbstverdauung des Darmes im Magen," Mitt. a.d. Grenzgebieten, 1910, 21, 143-153. Licini, C.: "Der Einfluss der Magensaft auf lebende Organgewebe bei gesundem und zerstörtem Peritonealüberzug," Bruns Beiträge, 1912, 82, 377-384.
187. Fenwick: cited by Moeller, l. c., 545. Litthauer: Virchows Archiv., 1908, 195. Clairmont, P.: "Ueber das experimentelle erzeugte Ulcus ventriculi und seine Heilung durch die Gastroenterostomie," Archiv. f. Klin. Chirurgie, 1908, 86, 1. Ribbert, H.: "Experimentelle Magengeschwüre," Frankf. Ztschr. f. Pathol., 1915, 16, 343. Pavy: cited by Moller, l.c., 545. Muller: cited by Moller, l.c. 545. Korte, W.: "Runden Magengeschwür," Dissert, Strassburg, 1875.

- Luzuki, T.: "Ueber experimentelle Erzeugung der Magengeschwüre," Arch. f. klin. Chir., 1912, 98, 632-648.
188. Disse: "Ueber die Blutgefäße der menschlichen Magenschleimhaut, besonders über die Arterien derselben," Arch. f. microsc. Anatomie, 1904, 63, p. 512-531.
189. Albert, G.: "Ein Beitrag zur operativen Behandlung der akuten Magenblutungen," Deutsche Zeitschr. f. Chir., 1914, 130, 398-412.
190. Fibich, R.: "Experimentelle Untersuchungen ueber die Einwirkung der Gastroenteroanastomose auf das ulcus ventriculi," Arch. f. klin. Chirurgie, 1906, 79, 900, Berl.
191. Panum: Virchows Arch., 1862, 25, 488.
192. Cohnheim, Julius, F.: Berlin, Hirschwald, 1877-1880. Allgemeine Pathologie, 1880, 2, 53.
193. Payr: "Experimente über Magenveränderungen als Folge von Thrombose and Embolie im Pfortadergebiete," Arch. f. Kl. Chir. Berl., 84, 799-854. Arch. f. klin. Chirurgie, 1907, 84, 793, u. 93, 436.
194. Hauser, G.: (Sein Vernarbungsprocess). Leipzig (not listed) Das Chronische Magengeschwür, 1883, 7 F. C. W. Vogel.
195. Redwitz: To be published, in Zieglers Beiträge.
196. v. Recklingshausen: Virchows Archiv., 1864, 30, 368.
197. Merkel: cited by Hauser, No. 194.
198. Hoffman: Inaug. Diss., Leipzig, 1900. Engelhardt, G. and Neck, K.: Deutsche Ztschrft. f. Chir., 1901, 58, 308. Sthamer, E.: "Zur Frage der Entstehung von Magengeschwüren und Leberinfarcten nach experimentelle Netzresectionen," Deutsche Ztschr. f. Chir., 1901, 61, S. 518. Busse, W.: "Über postoperative Magen und Darmblutungen," Arch. f. klin. Chir., 1905, 76, 122. v. Eiselsberg, Freiher: "Über Magen und Duodenal Blutungen nach Operationen," Arch. f. klin. Chir., 1899, 59.
199. Sprengel, O.: "Die Appendicitis," 1906, Stuttgart, F. Enke, Deutsche Chirurgie, Lief., 1906, 46. (Abschnitt Esbrechen.)
200. Hochstetter: Archiv. f. Anat. u. Entwickelungsgeschichte, 1887.
201. Yatsushiro, T.: "Zur Frage des retrograden Transportes im Pfortadergebiete," Virchows Archiv., 1911, 1912, 207, 236-257.
202. Nitsche, E.: "Magenblutung bei Appendicitis," Deutsche Zeitschr. f. Chir., 1902, 64, 180.
203. Reichard: "Drei Falle von todlicher parenchymatöser Magenblutung (aus der duringischen Abteilung des Augusta hospitales in Berlin,)" Münchener Med. Wochenschr., 1900, No. 22, 778 (Zwei Frauen).
204. Orth Johannes: Berlin, Hirschwald, Lehrbuch d. spez. path. Anatomie, 1887-1906, 1, 738.
205. Kaufmann, Edward: Berlin, Reimez, 1901, Lehrbuch d. specz. pathol. Anat., 3, Aufl., 384.
206. Ritter, A.: "Ueber den Einfluss von Traumen auf die Entstehung des Magengeschwürs," Ztschrft. f. Klin. Med., 1887, 12, 592.
207. Kienbock, R.: "Ein Fall von Zwerchfelhernie mit Rontgenuntersuchung," Zeitschr. f. klin. Med., 1907, 62, 321. v. Bonin: Bruns Beiträge, 1916, 99, 103.
208. Decker, J.: "Aus der Medicinischen Klinik zu Würzburg," "Experimentellen Beitrag zur Etiologie der Magengeschwüren," Berlin kl. Wochenschr., 1887, 21, 369.
209. Strohmeier, F.: "Die Pathogenese des Ulcus ventriculi, zugleich an Beitrag zur Frage nach den Beziehungen zwischen Ulcus und Carcinoma," Beitr. z. path. Anat. u. z. allg. Path., Jena, 1912, 54, 1-67. Zieglers Beiträge, 1912, 54, 1.

210. Nauner, C.: "Mykotisch—peptisches Magengeschwür," *Munchener med. Wochenschrift*, 1895, No. 38, 877.
211. Fritz, Mayer: "Ueber parenchymatöse Magenblutungen," *Inaug. Diss. Bonn*, 1912, I. Wurm, 47, p. 8°.
212. Chantemesse and Widal: cited by Moller, l. c., 555. Wurtz, R., and Lendet, R.: "Recherches sur l'action pathogene du bacille lactique," *Arch. med. exp.*, 1891, 3, 485. Besancon and Griffon: cited by Moeller, l. c., 555. Charrin: cited by Moller, l. c., P. 555. Letulle: *Compt. rend. Acad. Scient.*, 1888. Steinharter, E. C.: "A preliminary note on the experimental production of gastric ulcers by the intravenous injection of clumped colon bacilli," *Boston M. and S. T.*, 1913, 81, 169; *Inneres Kongress Zentralblatt*, 1911, 10, 210.
213. Singer, C.: "The production of ulcer of the stomach in the rat," *Lancet*, 1913, 2, 185, 279-281.
214. Turck, F. B.: "Fur Aetiologie und Pathologie des runden Magen und Duodenal Geschwures," *Zeitschr. f. exp. Path. u. Therapie*, 1909-1910, 7, 615.
215. Kuttner: *Chirurgenkongress*, 1913, v. 42. v. Haberer, H.: "Ulcus duodeni und postoperative peptisches Jejunalgeschwür," *Arch. f. klin. Chir.*, 1918, 109, 413, 566.
216. Breus: *Wiener med. Wochenschrift*, 1878, No. 28.
217. Gossmann: "Ueber das tuberculose Magengeschwür," *Grenzgebiete*, 1913, 26, 771. Keller, Katharina: "Zur Pathogenese und Therapie der Magentuberkulose," *Bruns Beitrage*, 1914, 88, 586. Zesas, D. G.: "Die Tuberculose des Magens," *Centralbl. f. d. Grenzgeb. d. Med. u. Chir.*, Jena, 1913, 17, 448-508. *Grenzgebiete*, 1913, 26.
218. Sjubimowa cited by *Chir. Kongressblatt*, 3, 529.
219. Rosenow, E. C.: "The production of Ulcer of the Stomach by Injection of Streptococci," *J. A. M. A.*, 1913, 61, 1947.
220. Gossmann, T. R.: "Ueber das tuberculoese Magengeschwür," *Mitt. a. d. Grenzgebieten*, 1913, 26, 771.
221. Wilms, M.: "Miliartuberculose des Magens," *Zentralbl. F. Pathologie*, 1897, Bk. 8, 783.
222. v. Cammerer: "Cited by Viktor Lieblein and Heinrich Hilgenreiner," "Die Geschwure und die erworbenen Fisteln des Magen Darmkanals," Stuttgart, 1905, F. Enke, 631 p.; *Forms L. 460 f.*, *Deutsche Chir.*, 1905.
223. Talma, S.: "Untersuchungen ueber Ulcus Ventriculi simplex, Gastromalaciæ und Ileus," *Ztschrift. f. Klin. Med.*, 1890, v. 17, Part 1, p. 10.
224. v. Yzeren, W. van: "Die Pathogenesis des chronischen Magengeschwures," *Zeitschr. f. klin. Med.*, 1901, 43, 181.
225. Lichtenbelt, J. W.: *Die Ursache d. chronischen Magengeschwurs*, Fischer, Jena, 1912.
226. Antonini, L.: "La resezione intratoracica laterale del vago nei suoi rapporti con la patogenesi dell'ulcera rotonda dello stomaco," *Riform. med.*, 1914, 30, 88, 116, Napoli.
227. Donati, Mario: "Ueber die Moglichkeit, das Magengeschwür durch Lasionen der Magenerven hervorzurufen," *Arch. f. Klin. Chirurgie*, 1904, 73, 908. Dalla Vedova, R.: "Experimentellen Beitrag zur Kenntniss der Pathogenese des Ulcus Ventriculi," *Archiv. f. Verdauungskrankheiten*, 1902, 8, 3, 2554, 411.
228. Singer, G.: "Zur radiologischen Diagnose des Magen und Duodenalgeschwurs," *Deutsche Med. Wochenschr.*, 1918, 17, 456.
229. Kobayashi, M.: "Ueber experimentelle Erzeugung von peptischen Erosionen" (*Stigmata ventriculi*), *Frankfurter Zeitschr. f. Pathol.*, 1909, 3, 566.



230. Kanamura, K.: "Ueber die experimentelle Erzeugung von Magengeschwüren durch nervenläsionen," Deutsche Zeitschr. f. Chirurgie, 1911, 109 (lit), 540.
231. Schiff: Unders z. Physiol. d. Nervensystems, 1885.
232. Ebstein, Wilhelm: "Experimentelle Untersuchungen ueber das Zustandekommen von Beutentravasaten in der Magenschleimhaut," Arch. f. experim. Pathol. u. Pharmakologie, 1874, 2, 183.
233. Gundelfinger, E.: "Klinische und experimentelle Untersuchungen ueber den Einfluss des Nervensystems bei der Entstehung des runden Magengeschwurs," Mitt. a. d. Grenzgebieten, 1918, 30, 189, 189-229.
234. Nagamori, Hikohachi: "Ueber experimentelle Erzeugung von Magen geschwüren beim Kanninchen durch Reizungen des Plexus coeliacus," Inaug. Diss. Wurzburg, 1910.
235. Klebs, Edwin, Berlin, Hirschwald: Handbuch d. path. Anatomie, 1869-1880, p. 185.
236. Cohnheim, Julius Friedrich, Berlin, Hirschwald: 1887-1880; Vorlesungen über Allgemeine Pathologie, 1880, p. 52.
237. Beneke: "Ueber die hemorrhagischen Erosionen des Magens (Stigmata ventriculi)," Verhandlung d. deutsch. path. Gesellschaft, Jena, 1908, 12, 284-294; Verhandl. d. pathol. Gesellschaft, 1908.
238. Hart: Grenzgebiete, 1916 or 1917, 31, 291 and 350. v. Bergmann, G.: "Ueber Beziehungen des Nervensystems zur motorischen Funktion des Magens. Zugleich Antwort auf Mittheilungen der Herren Eisler und Lenk," Münchener Med. Wochenschr., 1913, 169; Berl. kl. Woch., 1918, No. 23; Münchener Med. Wochenschr., 1913, 60, 2459. Januschke, H.: "Einige physiologische Gesichtspunkte in der Behandlung des Magengeschwurs und verwandte Zustände," Therap. Monatshefte, 1914, 28, 244. Westphal, K.-Katsch: "Untersuchungen zur Frage der nervösen Entstehung peptischer Ulcera," Mitt. a. d. Grenzgeb., 1916, 26, 391, u. D. Arch. F. Klin. Med., 1914 (Leipzig), 114, 327-395.
239. Roessle: "Zur Genese der Magen und Duodenalgeschwüre," München med. Wchenschr., 1912, 59, 1407; Mitt. a. d. Grenzgebieten, 1912-1913, v. 25.
240. Rosler: Med. Klinik, 1919, p. 1057.
241. Martins, F.: "Konstitution und Vererbung in ihren Beziehungen zur Pathologie," Konstitution-Vererbung-Berlin, Springer Verlag, 1914, 80, p. 267. Bauer, Julius: Konst. Disposit. z. inn. Krankheiten, Verlag. I. Springer, 1917, 8°, p. 586.
242. Quincke, H. and Dettweiler: "Ueber die Entstehung des Magengeschwurs," Deutsche med. Wochenschrift, 1882, No. 6, 79.
243. Silbermann, O.: "Vom Ulcus ventriculi rotundum," Deutsche Med. Wochenschr., 1886, No. 29, 497.
244. Futterer, Festschrift. f. Rindfleisch, 1907, p. 89.
245. Licini: "Ueber experimentelle Erzeugung von Magengeschwüren," Bruns Beiträge, z. Klin. Chir. Tubing, 1912, 79, p. 462-475.
246. Eppinger and Hess: "Zur Kasuistik der Atemstörungen by Tabes dorsalis," Wien. klin. Wchenschr., 1909, 22, 852. See also Eng. Zeitschr. f. inn. Med., 67-68, Die Vagotonie in v. Noorden's Samml. Kl. Abh. 1910, No. 9/10.
247. v. Bergmann, G.: "Ulcus duodeni vegetatives Nervensystem," Berlin kl. Wochenschr., 1913, 50, 2374-2379, a. 1918 and Westphal: Arch. f. klin. Med., v. 114, 2-97.
248. Lehmann, G.: (2) "Was leistet die Pharmakologische Prüfung in der Diagnostik der Störungen im vegetativen Nervensystem," (1) "Ulcus pepticum und Vegeta-

- tives Nervensystem," Berlin kl. Wochenschr., 1919, No. 33, 772. Zeitschr. f. klin. Med., 1914, 1915, 81, 52, 3-97.
249. Rutimeyer: Ueber die geographische Verbreitung des Ulcus ventriculi.
250. Bolton: Proceedings of the royal society of London, 1905, 74, 139; 1906, 77, 426; 1907, 79, 533; 1910, 82, 233.
251. Gundermann, W.: "Ueber experimentelle Erzeugung von Magen und Darmgeschwuren" Verhandlung d. deutsch. Gesellsch. f. Chir., Berlin, 1913, 42, 2 Theil, 54-67; Bruns Beitrage, 90, 1.
252. v. Redwitz, E. F., v. Redwitz: (2) "Weitree Beitrage zur chirurgischen Behandlung des Magengeschwur," (1) "Des pylorusfernen Ulcus ventriculi," Mitt. a. d. Grenzgebieten, 1914-1915, 28, 150. (2) Arch. f. klin. chir., 1918, 110.
253. Kausch, Walter; Bruns, P., et al, Editors, Handbuch d. prakt. Chir., 4, 1913, p. 265, v. 3.
254. Furstner, H.: "Zur Technik der Magenresection," Deutsche Zeitschr. f. Chirurgie, Leipzig, 1914, 128, 514-573. Hochenegg: "Gastroenterostomie oder Resection by Ulcus ventriculi," Wiener kl. Wochenschrift, 1910, 23, 52-54. Kocher, A.: "Ueber den Wert der Gastroenterostomie," Deutsche Zeitschr. f. Chir., 1912, 116, 183-225. Krabbel, M. and Geinitz, H.: "Beitrage zur Chirurgie der gutartigen Magenkrankungen," Grenzgebiete, 1914, 27, 859-911. Kuttner, H.: "Ulcus duodeni," Verhandlungen. d. deutsch. Gesellsch. f. Chir. Berl., 1913, 42, 2 Part, 37-53 (discussion), 1 Part, 64-68. Chirurgenkongress, 1914.
255. Brenner, A.: Zur Frage der Gastroenterostomie oder Resection bei pylorusfernen ulcer ventriculi," Wiener Klin. Wochenschr., 1913, 26, 1788-1790. Schwarz, K.: "Ueber penetricrende Magen und Jejunalgeschwure," Bruns Beitrage, 1910, 67, 96-128.
256. Brun, H.: "Magenchirurgische Probleme, insbesondere uber die Wirkung der Gastroenterostomie," Deutsche Zeitschr. f. Chir., 1915, 132, 511-528. von Redwitz (195). Kemp, S.: "Beitrag zur Pathologie und Therapie des Magengeschwures 2. Ulcus chron. juxtapyloricum, dessen Diagnose und Behandlung" Mittheil. a. d. Grenzgebiete der Med. and Chir. Jena, 1913-1914, 27, 436-478.
257. Plaskhe, S. (2) and Schur, H.: (1) "Die Bedeutung der Funktion des Antrum pylori fur die Magen Chirurgie. Ein Beitrag zur Behandlung des peptischen Geschwurs," Grenzgebiete, 1915, 28, 795-815. Kocher, Th.: "Die Chirurgische Therapie bei Magenleiden," Grenzgebiete, 1909, 20, 860.
258. Clairmont, P.: "Zur chirurgischen Therapie des Ulcus ventriculi," Mitt. a. d. Grenzgebieten, 1909, 20, Jena, 330-346.
259. Hornborg, A. F.: See No. 40, Skand. Arch. f. Physiol., 1904, 15. Latarjet, A. and Cade, A.: "Realization Pathologique du Petit Estomac de Pavdor," Journ. de physiolog. et. pathol. gen., 1905, 7, 221. Richet, Ch.: "Proprietes chimiques et Physiologiques du suc gastrique ches L'Homme et les animans," Journal de l'Anat. et de la physiol., 1878, 170. Beaumont, Wm.: 2 publications in English: "Experiments and observations on the gastric juice, and the physiology of digestion," Plattsburgh, Allen, 1833, and same, Boston, Lilly, 1834; Neue Versuche u. Beobachtungen uber den Magensaft u. s. w. Deutsch v. B. Luden, Leipzig, 1834. Kaznelon, Helene: "Scheinfutterungsversuche am erwachsenen Menschen," Pflugers Archiv., 1907, 118, 327.
260. Cohn, M.: "Die Gastrostomie im Roentgenbilde," Fortsch. a. d. Gebiete d. Roentgenstrahlen, 1914-1915, 22, 377-384, 4 pl.

## CHAPTER III

### PANCREAS

The pancreas has a double function. Its external secretion, which takes a prominent part in digestion is poured through the duct of Wirsung into the duodenum (1); its internal secretion is given directly to the blood and has a most important effect on the general metabolism. Our knowledge of the external secretion is linked especially with the names of Heidenhain (2) and Pawlow (3) while recognition of the internal secretion is indebted to v. Mering and Minkowski (4) (1889), who observed glycosuria with subsequent cachexia, after total extirpation of the pancreas, that is, they reproduced a typical diabetes mellitus.

The *external secretion* of the pancreatic juice may be studied in dogs by two methods, *viz.*, by suturing the opening of the excretory duct with its attached piece of duodenum to the skin, or better, by producing a duodenal fistula and providing a passageway for the bile after previous ligation of the common duct by suturing the gall bladder to the intestines (5). Stimulation to external secretion occurs principally, as far as we now know, when food passes through the duodenum, first, reflexly, through nervous influences, and second, by way of the blood from the action of absorbed secretin. The vagus and the splanchnics supply the pancreatic tissue, its blood vessels, and the autonomic centers, that is, the ganglion cells in the gland substance itself. Because of this very complicated innervation and because blood pressure changes play a very important part, the investigations of the effect of stimulation of these nerves on the external secretion, have lead to quite divergent results (6). In particularly careful experiments, Pawlow was finally able to consistently obtain a plentiful secretion of pancreatic juice by stimulation of the vagus; a scanty secretion followed stimulation of the sympathetic (see also Oppenheim, "Die Fermente," Volume I, fourth edition, p. 468). The most active stimulus to external secretion, however, is not carried to the pancreas through nervous paths, but by the blood after the absorption of a substance known as *secretin* elaborated by intestinal mucosa. The importance of this secretin was discovered by Bayliss and Starling (7), who demonstrated that there is first a prosecretin in the bowel mucosa, *i.e.*, a pre-stage of secretin, and that this is changed to secretin under the influence of the hydrochloric acid from the stomach. Then, according to Bayliss and Starling, the secretin thus formed is quickly absorbed by the

bowel and carried by the blood to the pancreas. The existence of a prosecretin has, however, recently been disputed (8) and the idea is expressed that the acid acts only as a solvent for secretin, and destroys erepsin, which inhibits secretin. Popielski (9) furthermore, thinks that secretin acts only through the nervous system; but this view has been disproved by Fleig's (10) experiments, which furnished positive proofs that secretin exercises its function by way of the blood stream. At the same time Fleig is willing to admit a nervous regulation. Secretion begins in about five minutes after hydrochloric acid enters the bowel.

[Doubts of the specificity of secretin and also of gastrin have been expressed from time to time. Recently, these have crystallized in work by Luckhardt which he reported in 1921. In very carefully performed experiments he has shown that secretin or gastrin may stimulate the pancreas or the gastric glands or both, and further that very efficient secretagogues may be prepared from other organs than duodenal or gastric mucosa.]

For studies of the histological changes occurring during activity and rest of the gland cells, the work of Heidenhain (2), Kuhne and Lea (12), and recently Bremer (13) may be consulted.

As an example of the nervous influence, Cohnheim (14) states that the mere offering of food causes a flow. Thus there is a psychological factor just as in the stomach. The character of foods passing through the duodenum also influences secretion for water as well as albumoses and oil lead to a scanty amount, while soap which is formed from oil stimulates the flow of larger amounts (5). Furthermore, the quantity secreted during a meal is dependent on the amount of gastric juice (15). It is larger after proteins than after carbohydrates and in the case of the latter substance, differs according to their kind and mode of preparation. But Wohlgemuth (16) disputes this, and states that the quantity is greater after carbohydrate feeding. Heineke (17) on the basis of these statements, advises that patients with pancreatic fistulæ be given such food as is ordered for diabetics.

Observations of the secretion of pancreatic juice in operated patients with fistulæ have been recorded by Schumm (18) and Glassmer (19). The important point has been brought out that there are no differences in the quality and quantity of pancreatic secretion in man and the dog.

The most important physiological substances in the pancreatic juice are the digestive enzymes. *Trypsin*, the knowledge of which we owe principally to Kuhne (20) is proteolytic, and breaks down proteins not only to pepton, but carries the cleavage as far as amino acids. In the gland, it is present in a pre-stage, usually called zymogen, and according to Pawlow (21) it is activated by the enterokinase present in the intestinal



lumen. It acts particularly well in a strongly alkaline medium, such as that found in the normal pancreatic juice. Activation from trypsinogen to trypsin can be accomplished not only by the succus entericus but also by certain bacteria (22); calcium salts (Delezenne (23)), pressed liver substance (Wohlgemuth (24)), and a number of colloids (Larguier des Banals (25)). By using special experimental methods, *e.g.*, the injection of pilocarpin, Camus and Gley (26) showed that the trypsin may be activated within the pancreas itself and thus there is a possibility that under certain circumstances, an active pancreatic juice may be secreted. Eberle (27) was the first to recognize that the lipase splits, not only neutral fats, but also lower esters into glycerin and fatty acids. The quantity present in the pancreas varies quite considerably and is said to occur in particularly large amounts in fasting animals (28). *Steapsin* when secreted is not a preenzyme but is active, although its activity may be increased considerably by the addition of bile acid salts (29).

The *diastatic* action of the pancreatic juice, *i.e.*, the splitting of starches to sugar, was first observed by Bonchardat and Sandras (30). It is found in varying degree in the pancreatic juice of all animals (31). Many experiments and clinical observations indicate that the amylolytic enzyme of the blood has a definite relation to the pancreatic amylase, because most of that in the blood has been secreted by the pancreas directly into that fluid. Thus it follows that after extirpation of the pancreas there is a diminution of this enzyme in the blood and an increase after ligation of the duct of Wirsung and the resultant stasis of the external secretion. Coincident with its increase in the blood, there occurs an increase in the urine and Wohlgemuth (33) on the basis of this finding, recommends its quantitative determination in the urine as a diagnostic help in obstruction of the duct of Wirsung.

Of the other enzymes of the pancreatic juice, the *nuclease* might be mentioned (34). This enzyme is of diagnostic importance since the nuclein test proposed by Schmidt (35) has, as a basis, its presence or absence; but it must be remembered that a nuclease is present in the intestinal mucosa also. The glutinase and casease which according to the newer investigations are probably identical with trypsin (see Oppenheimer, *l.c.*, pp. 442 and 445) the hemolysin (36) and the necrotising, blood pressure reducing substances which have as yet not been fully investigated, may be passed over.

According to the statements of Walther (37) (Pawlow), the quantity of the enzymes in the pancreatic juice varies considerably with the food. These statements of Pawlow and his school have, however, been sharply questioned, particularly by Popielski (6). Since the investigations of Walther were made before the zymogens (the pre-enzymes) were known,

his published figures cannot make any claim to absolute correctness, so that this point needs further investigation (38).

*Total extirpation* of the pancreas is followed by a diabetes, and the glycosuria is not a result of a nerve lesion, nor of absence of the external secretion, but it depends on a failure of some substance which is supplied by the gland directly to the blood stream. The diabetes following extirpation was discovered in 1889 by v. Mering and Minkowski (4) and at about the same time by de Dominici (39).

Considerable controversy arose immediately, as to whether this diabetes followed because the external secretory function of the pancreas was abolished, or the internal, or both. The crucial experiment was supplied by Minkowski (40) who transplanted the uncinate process of the pancreas of a dog under the skin of the abdominal wall, leaving a pedicle of vessels for its immediate nutrition. The pedicle was later severed, and the entire remainder of the pancreas removed. Diabetes did not develop, nor did glycosuria appear until the transplant had been removed. Death then resulted from a severe diabetes.

The appearance of sugar in the urine is a result of hyperglycemia, but, according to the work of de Meyer (41) there may also be an increased permeability of the kidneys to this substance. It is not positively known at just what place in the complex metabolism of carbohydrates the failure of the internal secretory function of the pancreas makes itself felt. There are, however, many single facts, most of which are confirmed by experiments, and the most important theories of pancreatic diabetes may be mentioned in short outline (42).

De Dominici's assumption (39) that diabetes resulted from the absence of the external secretion after extirpation of the pancreas, and Pflüger's that it is dependent on nervous regulation originating in the pancreas, have both been disproved by the experiments of Minkowski (40) mentioned above and those of Hedon (43) among others. It must be accepted at present, that there is a pancreatic hormone, which, according to Biedl, reaches the blood stream by way of the thoracic duct, for, according to his figures, when the fluid from the thoracic duct escapes through a fistula, a lasting glycosuria results in from 66 to 88 per cent. of the cases. That it occurs when this vessel is ligated during operations in its vicinity or when it is done intentionally, *e.g.*, in fat embolism (Wilms (44)), should also be borne in mind. Whether some enters the blood stream directly without passing through the thoracic duct is still an undecided question.

How the *pancreatic hormone acts in carbohydrate metabolism* is the next question for consideration. The present day theories may be divided into two large groups. It is believed, first, that the pancreas in some way takes a prominent part in the destruction of sugar and second, that it has

a regulatory influence in the synthesis of this substance. Further details may be found discussed by Biedl (42, p. 361). At present it may be concluded from the numerous experiments, many of them extraordinarily accurate, that not only sugar formation but sugar consumption in the tissues is altered after extirpation of the pancreas, and that the hyperglycemia is a result of this combined disturbance in carbohydrate metabolism along with involvement of other internal secretory glands.

There is also a diminution of antitrypsin in the serum after extirpation of the pancreas and Stawraky (45) believes this is responsible for the predisposition of diabetics to suppuration.

The debated question of whether internal secretion comes from the islands of Langerhans is not completely settled, but, from the anatomical point of view, many investigations (46) have shown that there are definite histological changes in those structures in the largest majority of diabetics. These may be of the nature of hydropic or hyalin degeneration, or of an inflammatory process with resultant atrophy, etc.; and their constancy makes it necessary to assume that at least a part of the internal secretion of the pancreas is provided by these structures. If the gland acini also take part in the internal secretion is an open question, to which many very carefully planned experiments have been directed (47). These have consisted chiefly of histological examinations after ligation of the duct or after the injection of substances to stimulate or inhibit secretion. The relation of the acini to the cells of the islands were then studied (42; p. 370). This was first done by Laguerre and his school but the details cannot be given. It must be admitted that the question has not been completely answered, although the theory has gained in probability. The same uncertainty surrounds the question of whether the islands take part in the external secretion (see Lombroso (48)).

Up to the present, the only internal secretory function of the pancreas which has claimed our attention has been that concerned in carbohydrate metabolism. But there is another field in which it exerts a profound influence, for the investigations of a number of workers have shown that fat absorption in the bowel is almost entirely suspended after total extirpation of the gland. But the splitting of fat is carried out approximately normally by the bacteria in the intestinal canal (49).

After extirpation, the absence of the internal secretion so dominates the clinical picture, that we cannot obtain a real perspective of the results brought about by absence of the external secretion. Experimental ligation of the ducts has been done many times (50) but the results were not always of value, because, especially in the dog, there are often many accessory channels, and ligation of the duct of Wirsung and even another wider duct may not be sufficient to exclude all pancreatic fluid from the

bowel. In order to be certain, it is necessary to cut all strands found between the gland and the intestine with the exception of the vessels.

Studies of the *metabolism* after complete elimination of the external secretion (as made particularly by Rosenberg and more recently by Holmberg) have shown that there is an early disturbance, in the utilization of protein, so that only about two-thirds of the nitrogen is absorbed. When later high grade destruction of the gland develops, the absorption of fat and carbohydrates also shows deviations from the normal.

Changes in the splitting of proteins and of nucleic acid are not demonstrable. It is not easy to determine whether, as Rosenberg assumes, ligation of the pancreatic ducts leads to an absorption of larger quantities of the enzymes and subsequent excretion into the bowel "like iron," or whether the absorption of proteins and fats is influenced chiefly by the internal secretory function (Lombroso). The former possibility helps explain the comparatively minor disturbances in the splitting and absorption of the food material after the operation, but both possibilities may readily occur. At any rate, the opinion of Lombroso has gained considerable ground, especially since the investigations of Fleckseder. The latter showed that fat digestion remains normal when the pancreas is implanted in the belly wall, by which procedure, of course, its external secretion is completely excluded.

These questions of the internal secretion, and its relation to the external secretion, are particularly important to the surgeon in injuries of the pancreas (51). Frequently it is a case of a transverse tear which has been sutured, but thus far, the manner in which the pancreas functions and its fate anatomically, after such suture, are entirely unknown. The same is true of pancreatic cysts and their treatment.

The *anatomical changes* which occur after ligation of the duct of Wirsung are first, a wide dilatation of the ducts, which are finally filled "with a clear, yellow alkaline fluid containing no enzymes" ((50) p. 403), and second a destruction of the gland cells, with gradual infiltration of connective tissue often dense enough to give the organ the consistency of cartilage. There are many collections of round cells and punctate hemorrhages in this fibrous tissue. As Kuhne and Lea (52) and recently Ricker, Natus (53) and Knape (54) have shown, the pancreas in living rabbits may easily be observed microscopically. Natus studied these changes after ligation of the ducts by this method.

According to the studies of Laguesse (55), W. Schulze (56), Ssoboleff (57) and others (on rabbits) the islands of Langerhans remain intact for a long time after ligation of the ducts, and this corresponds to the clinical observation that diabetes is usually absent in cases of pancreatic calculi



(see Lombroso (50)). In addition, the pancreas of young dogs has quite extensive powers of regeneration which extend also to the islands of Langerhans (58). Such observations have not been made on older animals.

The histological changes following long standing stasis of secretion are quite similar to the usual picture of chronic pancreatitis in man, as Hess (59) among others has pointed out. Barth calls attention particularly to the fact that in chronic pancreatitis just as in experimental ligation of ducts, the islands of Langerhans are spared at first. The studies of Natus (53) on the pancreas of living rabbits are of particular help in understanding the beginning stages of this disease. By no means, however, does *chronic pancreatitis* always depend simply on this stasis of the secretion; an infection carried by either the blood or lymph channels may play a far more important part. Unfortunately, we are not always in a position to determine, even at autopsy, the cause and the course of events in such cases. It might even have been the remains of a former acute pancreatic necrosis. To obtain a basis for the comprehension of the clinical picture, however, it is necessary to fall back on the conditions as found after ligation of the ducts. The failure of the external secretion in chronic pancreatitis may be occasionally demonstrated, according to Ad. Schmidt (61) by finding undigested muscle fibres and a fatty coating over the stools. Such findings are not constant; in fact, the diagnosis is very difficult and often cannot be made with certainty in spite of the many methods which have been proposed. This is perfectly clear when it is remembered that experimental incomplete ligation of the ducts (as performed by Rosenberg and others), leads to a sclerosis of a large part of the organ, but not to a recognizable alteration in metabolism.

According to Barth (60) the severe pains to which patients with chronic pancreatitis are subject, and which often lead to a mistaken diagnosis of gall stone colic are due to an involvement of the neighboring solar plexus or its branches (62).

From the therapeutic standpoint, it is usually assumed that chronic pancreatitis is caused by stasis of secretion and since it is also assumed that stasis of bile increases pancreatic stasis, free drainage of bile is established through a fistula of the gall bladder.

[That form of pancreatitis which is more or less localized in the head of the organ and is very frequently associated with cholelithiasis or at least with cholecystitis, has given rise to considerable controversy in regard to its etiology. That it is very important cannot be denied; the records of the follow up department in the Lankenau Hospital indicate that those patients who have this condition associated with their cholecystitis do not as a rule recover health or well being after operation as promptly nor as

certainly as those with cholecystitis alone. Suffice it to say that they complain of pain in the upper abdomen and continued digestive disturbances. The theory of the lymphogenous origin has been championed in this country by Deaver. In his clinical experience he has followed the train of events in this wise; cholecystitis, lymphadenitis at the junction of cystic and common ducts, lymphangitis and lymphadenitis along the common duct and finally pancreatic lymphangitis leading to sclerosis of the head of the organ. The close relationship of this part and the common duct is adequately explained on embryological grounds, and the lymphatics have been injected from the gall bladder. It is well known that infection of the gall bladder is very frequently present in its walls. On the other hand Archibald on the basis of experiments argues that the route of infection is via the common duct. A rise in pressure will force bile into the pancreatic duct and produce lesions in the gland. The sphincter of Oddi which closes the opening of the common duct is able to withstand quite considerable pressure, up to 600 mm. of water in dogs. Mechanical irritation, application of acid and other means are sufficient to throw this muscle into spasm, whence regurgitation of bile into the pancreatic ducts can ensue. It must be remembered, however, that the anatomical makeup of the common and pancreatic ducts varies, and until a very careful necropsy study of the arrangement of the ducts is made in cases of chronic pancreatitis the last word will not be spoken. Even one case of sclerosis of the head of the pancreas in which it is proved that bile could not have entered the pancreas via the common duct will be decisive. The opposite does not hold, of course. Even if it is shown that bile could have entered in this way, it does not follow that it necessarily did. Finally, if the lymph route is at fault, removal of the source of infection is indicated; if high pressure in the duct system is the cause, minimizing this is the proper procedure (63).]

Very great surgical interest is attached to the so-called *acute pancreatitis*, or better, *pancreatic necrosis*, first described by Balser (64). The characteristic anatomical picture of this disease develops quickly and positively; and leads, without surgical interference, to a rapidly fatal outcome. It consists first of a destruction of the gland accompanied by extensive hemorrhage within its substance, and second, of necrosis of the surrounding fatty tissue because of leakage of the pancreatic steapsin. These innumerable lentil-size areas of necrosis in the mesenteries and great omentum with their punctate, marble-white appearance, are so extraordinary that they have been the starting point of all the experimental work in this disease. It was doubtful if these fat necroses were related in any way to the pancreas until R. Langerhans (65) succeeded in reproducing them in the subcutaneous fatty tissue of rabbits by the injection of pancreatic juice.

He then demonstrated that they depended on the splitting of fat and the formation of a calcium salt of the liberated fatty acids.

Now that the fat necrosis is sufficiently explained by the action of the steapsin, the next question is, how is the steapsin liberated from the gland, in other words, how is the destruction of the pancreas brought about? Two opinions are in conflict on this subject, and there is much experimental evidence in favor of both (66). The one, momentarily the favorite of the majority of writers, declares that the destruction of the pancreas is brought about in the same way that the fat necrosis is produced, *viz.*, by the activities of the pancreatic enzymes, particularly the trypsin. Chiari (67), therefore, speaks of an "intravital self-digestion." The same objection, however, is present as that in gastric ulcer. How does it happen that the pancreas suddenly becomes vulnerable to the action of its own enzymes? The views are divided on this point. Polya (68) and Kirchheim (69) believe that the toxic action is caused by the trypsin. Ricker, Natus, and Knape after observing the living pancreas in rabbits, reach the conclusion that the trypsin has nothing to do at first with the destruction of the gland. They showed experimentally how readily the pancreas reacts with stasis and hemorrhage to all sorts of irritations, and believe that in the explanation of the severe hemorrhage in pancreatic necrosis, the trypsin plays at most a secondary role. More important than this enzyme trypsin, according to the investigations of Knape, are the salts in the pancreatic juice. Knape believes that as soon as pancreatic juice has the opportunity of entering the surrounding tissues from the ducts, its salts exert such an intense irritative effect on the vasomotor nerves that severe hemorrhage into the pancreas occurs. The immediate stumbling block in this idea is the natural question, how can the pancreatic juice escape into the surrounding tissues in the first place? It might in high grade stasis, but in pancreatic hemorrhage, this condition is usually not found, at least as far as the pathological material goes. It is possible, of course, that a stasis of secretion can occur from a cause not readily demonstrable at autopsy such as a spastic closure of the sphincter of Oddi, as Archibald (70) concludes from various experiments. Once more, Knape states that some sort of a nervous stimulus arising in any part of the body may initiate spasm in the pancreatic vessels and be followed first by a small localized area of necrosis and second by the escape of the strongly irritant pancreatic juice after which destruction of the gland proceeds. He observed something similar in rabbits. The primary factor would, therefore, be reflex vessel spasm, just as in gastric ulcer. He points to innumerable cases in the literature in which such pancreatic necrosis is said to have arisen reflexly from hanging, choking, lifting heavy weights, severe hemorrhages, etc. He himself had observed a man who while swimming, was seized

with an acute pancreatitis with anatomically extensive destruction of the organ. The man was drowned, and this shows how extraordinarily rapid the hemorrhage may be. Actually the assumption of a reflex process may not be far wrong.

Indeed, even before the work of Ricker and his pupils, other writers had expressed the opinion that the destruction resulted from a change in blood supply. This was of course a very logical idea and corresponded very well with the views on the formation of gastric ulcers. Appropriate experiments were performed by Hildebrand (71), Payr and Martina (crushing of the pancreas) (72), and many others (for lit. see Guleke). Those of Bunge and Guleke (73) yielded the best results. They frequently produced anatomical changes very much resembling human fat and pancreatic necrosis by the production of venous thrombosis or by the injection of paraffin, oil, etc. into the arteries. The clinical case of Schultze (74) in which an aneurism of the pancreatico-duodenal artery was found as the basis of a pancreatic necrosis illustrates the value of these experiments.

Then a second group of writers expresses the opinion that the most important factor in the destruction of the pancreas is the trypsin, which of course must first be activated. We have already seen that the enterokinase is the normal activator of this substance. But dying cells, such as leucocytes, bacteria, etc. may also perform this service. To bring about such activation within the gland itself, Korte (75) injected a small amount of intestinal contents directly into the parenchyma, and Hlava (76) and Carnot (76) used pure cultures of bacteria for the same purpose. The changes obtained in this way, however, showed no similarity to human pancreatic necrosis. They usually found circumscribed abscesses, hemorrhages, scars, and sparsely scattered fat necrosis from which the only conclusion that could be drawn was that the pancreas was relatively immune to infection. The human type was much more closely imitated by the injection of intestinal contents, bacteria, bile, blood, sodium chloride, fats, soap, oils, fatty acids, etc., into the excretory ducts. It must always be emphasized however, as Knape and Ricker especially have done, that these experiments bring both activation of pancreatic juice and tissue injury into play, and the latter may very well act by way of reflex constriction of vessels. This idea is shown especially well in Rosenbach's experiments in which he sutured the pancreas into the intestine and found that digestion of the gland occurred only if there was an injury produced at the same time. It may therefore be concluded with certainty that even the activated trypsin is unable to digest the living pancreatic tissue. But the fact remains that the injection of these various substances into the pancreatic ducts, has actually yielded changes



which are entirely comparable to the anatomical and clinical pictures of human pancreatic necrosis. They are, therefore, the most important of those mentioned. Seidel's experiments have shown that duodenal contents may enter the duct of Wirsung, and with the help of steapsin and activated trypsin, produce typical pancreatic and fat necrosis in spite of the sphincter of Oddi. These results were obtained by ligating the duodenum after a previous resection of the pylorus and posterior gastroenterostomy. A clinical case which illustrates the possibility of the entrance of intestinal contents is reported by Simmonds (77). A round worm was found in the pancreatic duct in acute pancreatic necrosis.

It is well to remember that the anatomical make up of Oddi's muscle is varied and its tonus also varies considerably in different individuals (dogs) (78).

[In addition, the entrance of the pancreatic duct into the common duct varies in a very important manner not only in species but in the different individuals of the same species (man and animals) (79).]

To sum up; on the basis of the experiments mentioned, we may conclude that fat necrosis occurs when the pancreas is injured and activated pancreatic juice is set free, perhaps the latter is not even necessary. Experimentally, these preliminaries can be completed by a disturbance in the blood supply as well as by the introduction of intestinal contents into the ducts. At present, it is not possible to determine the mode in man and we are able to judge just as little of the possibly far reaching importance of the observation of Fischlers (80) who found that Eck-fistula dogs are particularly susceptible to pancreatic necrosis.

Now that the anatomical changes in pancreatic necrosis have been partially explained, there still remains the problem of how the severe and fatal clinical course is produced. According to Maragliano (81) there exist the following possibilities.

- I. It may be an infection or an irritation of the peritoneum.
- II. An intoxication from soaps.
- III. An intoxication from enzymes.
- IV. An intoxication from substances, not identified, but formed in the disintegrating pancreas.

Bergmann and Guleke (82), who have worked extensively on this problem, were formerly of the opinion that death in pancreatic necrosis is due to trypsin poisoning, but recently they have reached the belief that the intoxication is not due to trypsin alone, but to a varied number of substances arising in the autolyzed pancreas. Doberauer (83) holds the same opinion. V. Bergmann and Guleke believe further they could obtain an immunization of their experimental animals against the fatal effect of autolyzed pancreatic substance by previous injections of trypsin.

## LITERATURE TO PANCREAS

1. See Heiberg: Die Krankheiten d. Pankreas, Wiesbaden, 1914 (Lit.). Lit. s. Babkin, Die äussere Secretion d. Verdauungsdrüsen, Springer, 1914.
2. Heidenhain: Hermann's Handbuch, 1883, 5, 1.
3. Pawlow: Arbeit d. Verdauungsdrüsen, 1898.
4. v. Mering: Zentralbl. f. Klin. Med., 1889, p. 393; Arch. f. exp. Path. u. Pharmacol., 1890, 26.
5. Cohnheim u. Klee: Zur Physiologie. d. Pankreas, Sitzungsbericht d. Heidelberger Akad. d. Wissensch., 1912, 3.
6. Popielski: Pflügers Archiv., 1901, 86, p. 215. Pawlow: Nagels Handbuch d. Physiol., 1906, 2, p. 737.
7. Starling and Bayliss: Zentralbl. f. Physiol., 1901-1902, 15, 23 and Journ. of Physiol., 1902, 28, p. 325.
8. Salou: J. de Physiol. Pathol. gen, 1912, 14, p. 509. Gley: also Oppenheim, p. 471, J. de Physiol. Pathol. gen, 1912, 14, p. 241-530.
9. Popielski: Pflügers Archiv., 1907, 120, 451.
10. Fleig: Zentralbl. f. Physiol., 1902, 16, p. 24 and Arch. gen de Med., 1903, 80, 1473.
11. Luckhardt, A. B., Henn, S. C. and Palmer, W. L.: "On the specificity of gastrin and pancreatic secretin," Am. J. Phys., 1922, 59, 457.
12. Kuhne und Lea: Unter aus d. physiol. Inst. Heidelberg, 1878, p. 448.
13. Bremer, F.: "Contribution a l'etud histophysiologique de la secretion externe du pancreas chez la chien (note preliminaire)," Ann. et bull. de la Soc. roy. des sciences med. et natur. de Bruxelles, 1913, 71, 82.
14. Cohnheim: Münchener med. Wochenschrift, 1907, p. 2581.
15. Schlagintweit, E. u. Stepp, W.: "Studien über die Pankreassekretion by Sekretionsstörungen des Magens nach experimenten am Dauerfistelhund," Deutsches Arch. f. Klin. Med., 1913, v. 112 und Münch. med. Wochenschr., 1913, 60, 1865-1867.
16. Wohlgemuth: "Untersuchungen ueber das Pankreas des Menschen," Berliner klin. Wochenschrift, 1907, 44, 47-51.
17. Heineke, H.: "Zur Behandlung der Pankreasfisteln," Zentralbl. f. Chir., 1907, 34, 265-667.
18. Schumm: Ztschft. f. phys. Chemie, 1902, 36, p. 292.
19. Glassmer: "Ueber menschliches Pankreassekret," Ztschrft. f. physiol. Chemie, 1903, 40, p. 465.
20. Kuhne: Virchows Arch., 1867, 39, p. 130.
21. Pawlow: Nagel's Handbuch, 2, p. 731.
22. Hekma, E.: "Ueber die Umwandlung des Trypsin-Zymogens in Trypsin," Arch. f. (Anat.) u. Physiol., 1904, p. 343-365. Delezenne: Compt. rend. de la Soc., Biol. 54, p. 1989. Breton, M.: "Sur la role kinasique des microbes normaux de l'intestin, particulierement chez l'enfant," Compt. rend. de la Soc. Biol., 56, p. 35.
23. Delezenne, C.: "Nouelle observations sur la specificite des sels de calcium dans la formation de la trypsine," Compt. rend. de la Soc. de Biol., 63, p. 274.
24. Wohlgemuth: Biochem. Ztschrft., 2, p. 264.
25. Larguier des Banals: "Activation du suc pancreatique pur sous l'influence combinee des colloides et des electrolytes," Compt. rend. de l'Acad., 141, p. 144.
26. L. Camus und E. Gley: "Rechershes sur la secretion pancreatique; variations de l'activite physiologique du suc pancreatique," Journ. physiol. path., 1907, v. 6, p. 987.

27. Eberle: *Physiol. d. Verdauung*, Wurzburg, 1854.
28. Grutzner: *Pflugers Arch.*, 1876, 12, 285.
29. Magnus, R.: "Die Wirkung synthetischer Gallensauren auf die pankreatische Fettspealtung," *Ztschrft. f. physiol. Chemie*, 1906, 48, p. 376.
30. Bonchardal und Sandras: *Compt. rend. Soc. Biol.*, 20, 1845, 143, p. 1085.
31. Langsdorff: *Arch. f. (Anat. u.) Physiol.*, 1879, p. 1. Lepine und Barral: *C. r. de l'Acad. des Sciences*, 1891, 113, p. 729. K. Moeckel und Rost, F.: "Ueber den Ursprung und die Bedeutung des amylolytischen Blutferments," *Ztschrft. f. physiol. Chemie*, 1910, 67, p. 459. Schlesinger, W.: "Zur Kenntniss des diastatischen Fermentes im Blute," *Verh. d. 25 Kongr. f. inn. Med.*, 1908, p. 501. Wohlgemuth, I.: "Ueber die Sekretion von Pankreasfisteln und ihre Besinflussung durch antidiabetische Diat; Bemerkungen zu den Arbeit von F. Kempf." *Deutsche Med. Wochenschrft.*, 1908, p. 765, und *Bioch. Ztschft.*, 1909, 21, p. 381. A. Clerk und Loeper: "Influence de la ligature du canal pancreatique sur le pouvoir amylolytique du sang," *Compt. rend. soc. Biol.*, 1909, 66, p. 871.
32. Rosenberg: *Inaug.-Diss.* Tubingen, 1890.
33. Wohlgemuth, I.: "Beitrag zur funktionellen Diagnostik des Pankreas," *Berliner klin. Wochenschrift*, 1910, part 3.
34. Sachs: *Ztschft. f. physiol. Chemie*, 1906, 46, p. 336.
35. Schmidt, A.: "Funktionelle Pankreasacheir," *Deutsches Arch. f. Klin. Med.*, 1906, 87, 451-478.
36. Wohlgemuth: *Bioch. Ztschrft.*, 4, p. 271. Friedemann, U.: "Ueber ein komplexes Hemolysin der Bauchspeicheldruse," *Deutsche med. Wochenschrift.*, 1907, No. 15, 585-588.
37. Walther: *Arch. des Sciences biol. de St. Petersburg*, 1899, 7, parts 1 and 2.
38. Cohnheim: "Die Physiologie der Verdauung und Ernährung 23 Vorlesungen fur Studierende und Aerzte-Berlin u. Wien, 1908, Urban Schwarzenberg, 492, p. 80. Die Physiologie der Verdauung usw., 1908, p. 81.
39. De Dominici: *Munchener Med. Wochenschrift.*, 1891.
40. Minkowski: *Arch. f. exp. Pathol. u. Pharmakol.*, 31, 1893.
41. De Meyer: *Arch. int. de Physiol.* 9, 1910, p. 101. Cited by Biedl. *Innere Sekretion*, Bk. 2, p. 351.
42. Anofuhlrl: *Lit. cf. Biedl. Innere Sekretion*, 1913, 2, 351. Biedl. Arthur: *The internal secretory organs, their physiology and path.*, London, 1912, Bale, Sons and Danielson, 594 p. 8°.
43. Hedon: *Arch. de med. exp.*, 1892, p. 617.
44. Wilms: *Chirurgen kongress*, 1910.
45. Stawraky, W.: "Zur Frage nach der fermentativen, Tatigkeit des Blutes und der Gewebe bei Pankreasextirpation. 1. Ueber das Antititrypsin," *Ztschrft. f. physiol. Chemie*, 1914, 89, 381-407.
46. Heiberg, K. A.: "Die Entstehungsweise der Inselveranderungen und ihr Verhalten bei Diabetes mellitus," *Zeigler's Beitrage z. path. Anat.*, 1911, 51, p. 178. Weichselbaum, A.: "Ueber die Veranderungen des Pankreas bei Diabetes mellitus," *Wiener Klin. Wochenschrift.*, 1911, 24, p. 153-159. Lubarsch: "Pathologie des Diabetes," *Jahresk. f. arzth. Fortbildung*, 1911, 1, 57-67.
47. See Heiberg, *Ergebn. d. Anat. von Merkel-Bonnet*, 1909, 79 und Gelle, *ibid.*, 1912, 2, 20, according to Weichselbaum (*Wien. Klin. Wochenschrft.* 2, p. 155) regeneration of destroyed islands takes place only from ducts.
48. Lombroso, U.: "Die Gewebelemente welche die innere Funktion des Pankreas besorgen," *Ergebn. d. Physiol.*, 1910, 9, 1-89.

49. Escherich: Die Darmbakterien des Sauglings, p. 158.
50. Holmberg: Dissert. St. Petersburg, 1913, Ref. Chir. Kongressbl., Vol. 4, p. 831.  
Lombroso, U.: "Zur Frage ueber die innere Funktion des Pankreas mit besonderer Rücksicht auf den Fettstoffwechsel," Arch. f. exp. Pathol., 1907, 56, p. 357 u. Ergebn. d. Physiol., 9, page 1. Rosenberg: Pflügers Arch., 1898, 70, p. 371. Fleckseder, R.: "Ueber die Rolle des Pankreas bei der Resorption der Nahrungsstoffe aus dem Darne," Arch. f. exp. Pathol. u. Pharm., 1908, 59, 407-419.
51. Garre, C.: "Totaler Querriss des Pankreas durch Naht geheilt," Beitrage z. klin. Chir., 1905, 46, 233-340. Homeyer: Münchener med. Wochenschrift, 1907. Heineke, H.: "Ueber Pankreasrupturen," Arch. f. Klin. Chir., 84, 1112-1134.
52. Kuhne und Lea: Untersuch. a. d. physiol. Institut. Heidelberg, 1882, 2.
53. Natus, M.: "Beitrage zur Lehre von der Stase nach Versuchen aus Pankreas des lebenden Kaninchens." "Versuch einer Theorie der chronischen Entzündung auf Grund von Beobachtungen am Pankreas des lebenden Kaninchens und von histologischen Untersuchungen nach Unterbindung des Ausführungsganges," Virchows Arch., 1910, 199-202, 417-471.
54. Knappe, W.: "Deutsche Zeitschrift. f. Chir., 121 und Virchows Arch. 206.
55. Laquesse, E.: "Ilots de Langerhans et secretion interne," Compt. rend. de la Soc. de Biol., 59, p. 368.
56. Schulze: Arch. f. Anatomie and Entwicklungsgeschichte, 1900, 56.
57. Isoboleff: Virchows Arch., 168.
58. Mora, Henri: "Pancreatectomies chez les jeunes chiens, leur influence sur le developpement et sur la glycolyse. These de Paris, 1913, Vigot Freres.
59. Hess, O.: "Pankreas necrose und Chronische Pankreatitis," Mitth. a. d. Grenzgebieten, 1909, 19, p. 661.
60. Barth: "Ueber indurative Pankreatitis," Arch. f. Klin. Chir., 1904, 74, 2.
61. Ad. Schmidt: Lit. to chronic pancreatitis: Fr. Muller. Deutsches Arch. f. Klin. Med., 1887, 12, Ad. Schmidt, Grenzgebiete, 1914, 26 und Arch. f. Klin. Med. 87, 1906, Guleke, Ergebn. f. Chir. v. 14, Gross, Deutsches Arch. f. Klin. Med. v. 108, 1912, p. 106, Riedel, Berliner, Kl. Wochenschrift, 1896, No. 1 a. 2, Barth. Arch. f. Kl. Chir. v. 74, Hess, Mitt. aus d. Grenzgebieten, 1909, v. 19, Ehrmann, Zeitschrift. f. klin. Medizin v. 69, Truhart, Pancreaspathologie Wiesbaden, 1902.
62. Schmieden, V.: "Ueber die Zirrhose des Pankreas," Münchener Med. Wochenschrift, 1906, 53, 2289-2292.
63. Archibald, E.: Surg. Gyn. and Obst., 1919, 28, 529. Deaver, J. B. and Sweet, J. E., J. A. M. A., 1921, 77, 196.
64. Balser: Virchows Arch., 1882, 90.
65. R. Langerhans: Festschrift. assistenten f. Virchow, 1891.
66. Natus, M.: "Beitrage zur ihre von der Stase nach Versuchen am Pankreas des lebenden Kaninchens," Virchows Arch., 1910, 199-202. Ricker, G.: "Zuratz ueber die Folgen der Unterbindung des Ausführungsganges der Bauchspeicheldrüse, etc.," Bruns Beitrage 87, p. 729. Knappe: "Die Pankreasemorrhagie," Virchows Archiv., 106 und Deutsche Zeitschrift. f. Chir., 1913, 121.
67. Chiari: Verhandlungen der Deutsch. path. Gesellschaft., 1901, 5.
68. Polya, E.: "Ueber die Pathogenese der akuten Pankreaserkrankungen," Mitt. a. d. Grenzgebieten, 1912, 24, p. 49.
69. Kirchheim: Arch. f. exp. Pathol. u. Pharmak., 1913, 74.
70. Archibald, Edward: (1) "Ideas concerning the causation of some cases of pancreatitis," Canad. J. M. and S., Toronto, 1913, 33. (2) "Experimental Production of



Pancreatitis in Animals as a result of the resistance of the common duct sphincter," *Surgery, Gynecology and Obstetrics*, June, 1919, No. 6, 529-545, 1 pl. 17 Internat. med. Congress, London, 1913.

71. Hildebrand: *Zentralbl. f. Chir.*, 1895 and *Arch. f. Klin. Chir.*, 57.
72. A Payr und Martina, E.: "Experimentelle Untersuchungen über die Aetiologie der Fettgewebnecrosen und der Leberveränderungen bei Schädigung des Pankreasgewebes," *Deutsche Zeitschrift. f. Chir.*, 1906, 83, 189-193.
73. Guleke, N.: "Ueber die experimentelle Pankreasnekrose und die Todesursache acuten Pankeasnekerose und die Todesursache bei acuten Pankreaserkrankungen." "Die neueren Ergebnisse in der Lehre der akuten und chronischen Erkrankungen des Pancreas, mit besonderer Berücksichtigung der entzündlichen Veränderungen," *Ergebn. d. Chr.*, 1912, 4, p. 408 and *Arch. f. klin. Chir.*, 1906, 78, 1908, 85. Bunge: *Arch. f. klin. Chir.*, 1903, 71, p. 726.
74. Schultze, W.: "Ueber zwei Aneurysmen von Baueingeweidearterien; zugleich ein Beitrag zur Aetiologie der Pankreas blutungen," *Zieglers Beitrage*, 1905, 38.
75. Korte: *Berliner Klinik.*, 1896, December.
76. Hlava: cited by Polya, *Mitt. aus d. Grenzgebieten*, 24, p. 49. Carnot: *These de Paris*, 1898.
77. Simmonds: *Deutsche med. Wochenschrift*, 1915.
78. Rost, F.: "Die funktionelle Bedeutung der Gallenblase; experimentelle und anatomische Untersuchungen nach Cholecystectomy," *Mitt. a. d. Grenzgebieten*, 1913, 26, p. 759.
79. For literature and discussion of the surgery see Sweet, J. E.: *Internat. Clinics*, 1915, 4, 293.
80. Fischler, F.: *Deutsches Arch. f. Klin. Med.*, 100 und *Grenzgebiete*, 1913, 26, 4, p. 103.
81. Maragliano, D.: "Le causauella morte per necrosi pancreatica," *Policlinica*, 1912, 19.
82. Guleke, N.: "Ueber subcutane Pankreas verletzungen," *Munchener med. Wochenschrift*, 1910, p. 1673; *med. Wochenschrift*, 57, 75-79. v. Bergmann: "Die Todesursache bei akuten Pankreaserkrankungen," *Zeitschrift. f. exp. Pathol. u. Therapie*, 1906, 3, 401-424.
83. Doberauer: "Ueber die sogenannte acute Pancreatitis und die Ursachen des schweren oft todlichen Verlauf derselben," *Bruns Beitrage*, 48, u. *Chirurgenkongress*, 1906, 456-515.

## CHAPTER IV

### LIVER AND GALL BLADDER

The liver, the physiological importance of which is indicated by its size, is interposed between the intestines and the greater circulation and serves to elaborate the energy values which enter the body as food (1). The liver has been compared to a sorting room, or a bank—well-selected comparisons since they imply that a division and purposeful reconstruction of the many food substances which enter by way of the portal system, take place here. But to these remarks might be added that warm blooded animals can tolerate extensive elimination of liver activity; as, for example, after establishing an Eck fistula (anastomosis between inferior vena cava and portal vein, ligation of portal vein (see later)).

The first and the most important place of *metabolism* must therefore be sought in the liver. *Cessation of function*, or what amounts to the same thing, its experimental elimination, can lead to a flooding of the circulation with substances which, although formed in the body from foodstuffs, are deleterious, and if not thrown off, poisonous. The liver regulates these metabolic processes by means of numerous enzymes, some contained in its own cells, and others received by way of the circulation, as for instance, from the pancreas. The different stages of metabolism within the liver are not carried on one by one, but they overlap in ways unknown in detail, making it still more difficult to grasp the complicated functions of this organ. Thus far, there is no evidence that these various functions take place in different sections of the liver as some French authors (see Hess-Serege (2)) claim, but it is remarkable that certain diseases seem to prefer special parts.

Tropical liver abscesses are found almost exclusively in the right lobe, while cirrhosis usually begins in the left lobe (3). Glenard and Serege's opinion, that the functions of the two lobes are independent of each other, to a certain degree, cannot be accepted at present. Nevertheless, there is a possibility, especially from facts in its pathological anatomy, that certain portions possess their own definite functions. If this were true, it would be of great importance to the surgeon, but such an assumption has no supporting evidence at present.

We know from the experiments of Gluck (4) and Ponfick (5) that rabbits easily tolerate the removal of two-thirds of the liver. The livers of the operated animals have a *very active regenerative power* so that after

a short time the remaining portion is doubled in size (6), possibly because the original amount of blood with the original vascular tonus flows through a much smaller amount of liver tissue. This hyperemia governs growth, and the cells cease to grow as soon as equilibrium is established between the inflow of blood and the growth of tissue. It is desirable to investigate this interesting theory experimentally. This regenerative power is found in man also, as for instance, in echinococcus cysts and other affections which destroy liver tissue mechanically.

These regenerated cells seem to function, although no investigations of changes in metabolism after partial resection have been published. The investigations of Gluck and Ponfik were confined to anatomical facts.

In Ponfik's experiments the other organs of the animals showed a comparatively slight injury. There was chiefly congestion in the abdominal organs, leading to considerable enlargement of the spleen.

We may now briefly review the various functions of the liver.

First, it has special importance in *carbohydrate metabolism*. We owe to Claude Bernard (7), among many other things, the demonstration that the liver stores carbohydrates in the form of glycogen, which it then changes into sugar and supplies to the body according to requirement. We cannot discuss in detail how this occurs, or by what enzymes it is accomplished (1). There is a rather lively controversy, supplemented by many carefully planned experiments concerning whether the body elaborates glycogen from substances other than carbohydrates, *i.e.*, from fats and proteins (8). This question, which is of special interest in the treatment of diabetes, has been generally answered to the effect that the liver does form glycogen from proteins, and perhaps from fat also. For this reason, it is now generally conceded that not merely carbohydrates but also proteins must be reduced in diabetics. For the surgeon, carbohydrate metabolism in the liver is of special interest, because its disturbances, which are comparatively easily demonstrated, are at present the most important diagnostic sign of liver lesions. The reduced tolerance to galactose is probably the most frequent. In simple obstructive jaundice, it is not present, but it is found in every icterus resulting from injured liver cells (9).

The importance of the liver in relation to the *anabolism and catabolism of proteins* is also not trivial. Proteins, broken down in the intestines to amino acids, are practically all carried into the body by the blood circulation, not by the lymph channels, which means they encounter the liver by way of the portal vein. Since these split products have not yet been demonstrated in the blood of the portal vein, it is assumed that the amino acids are synthesized in the bowel into complete protein molecules

and pass as such to the liver (10). The findings of Abderhalden and London (11), who replaced the food proteins given to Eck-fistula dogs by completely split proteins and yet had nitrogen equilibrium, support this view. How far the liver participated in this phase of the protein metabolism is by no means clear. Fischler on the basis of his experiments, believes the liver plays a prominent role in this process.

[That the blood contains amino acids and that they increase markedly during digestion has been clearly shown. The normal concentration of about 0.1 per cent. may be nearly doubled in the portal blood of dogs after a heavy protein meal; furthermore, there is a greater fall in the amounts of amino acids during their passage through the liver (difference between portal and hepatic vein blood) than during passage through the entire remainder of the body (difference between arterial and vena cava blood) (12).]

To the surgeon, this question is very important, especially because the loss of a part of the liver function through Eck's fistula may be serious (see later). The catabolic products formed from the protein molecule are dangerous and poisonous to the body; thus, for example, the ammonium salts formed by the splitting of proteins are converted into urea, and sent into the greater circulation in a non-toxic form (13). Blood from the portal vein is very rich in ammonium salts and if it is conducted directly into the vena cava, as in an Eck fistula, it may result in symptoms of ammonia intoxication, which, however, is not usually fatal (see later). The details of the formation of urea from protein are still obscure and they cannot be discussed here (14).

The liver is also concerned in *purin metabolism* which, of course, is merely a subdivision of protein metabolism. Proteins are classified into simple and compound proteins. Nucleo-proteins belong to the latter group, and are split into nucleic acid and a protein moiety by enzymes elaborated in various organs. Nucleic acid is broken down by enzymes through the various purin bases to uric acid which is quickly split further. As is well known, the disease "gout" is a disturbance of purin metabolism and we differentiate "renal" gout from "true gout." In the former, after increased formation of uric acid, the kidneys do not eliminate at a rate sufficient to prevent its accumulation in the blood and deposit in various tissues; in the latter, the disturbance results from a defective enzymic catabolism of purin bodies. Since enzymes which are active in the catabolism of nucleins (uricolytic ferments, etc.) have been found in the liver, although only in autolysis, and since it has been shown that the urine of Eck fistula dogs contains five times the normal quantity of uric acid, a number of writers believe the liver has considerable importance in gout, an opinion which is not generally accepted (1), (15).



Some of the ingested *fat* also traverses the liver, but by far the larger quantity enters the circulation through the chyle channels. As Fischler (1) expresses it, the liver has transferred its function in fat absorption to the intestine, since the bile formed by the liver is necessary to change fat into a water soluble form.

The fats reaching the liver may be stored there, but they may also undergo a vaguely understood alteration as shown by their participation in the formation of acetone bodies. Histologically, fatty acids have not been demonstrated in the liver (Fischler). Part of the fatty bodies, especially cholesterol is excreted in the bile, the other portion is added to the general metabolism after it undergoes a very complicated analysis and re-synthesis (16).

The *detoxifying property* of the liver, mentioned above, is active not only in reference to proteins, but to all sorts of ingested substances, which by conjugation, splitting, or in some other way, are made harmless to the organism. This applies especially to alkaloids, which for this reason are quickly fatal if introduced subcutaneously, but are comparatively harmless if taken by mouth when they can enter the liver by way of the portal vein. Schiff (17) found that a dose of nicotine which quickly killed a frog, deprived of its liver, did not even poison a normal one; in the same manner, a mammal may be quickly killed by injecting strychnine, morphine and other poisons into the greater circulation, while the same dose injected into a mesenteric vein is harmless (lit. see Wohlgemuth (14), p. 196).

Of course, this detoxifying process is not without its effects on the liver, and often its service rendered to the organism as a whole brings about its own destruction. This is evidenced anatomically, by the fatty degeneration following poisoning by phosphorus, alcohol, phloridzin, and a number of infectious diseases; by the loss of glycogen and finally by central necrosis of the lobules.

The contention of whether the fatty liver in *phosphorus poisoning* is a result of degeneration or infiltration, may be decided by the investigations of Lebedeff (18) in favor of the latter. He starved dogs until they had lost practically all of their fat and then fed them with linseed oil and meat, poisoning them at the same time with phosphorus. Their liver cells contained linseed oil, but no dog fat; consequently there could not have been a change of protein into fat, or as it is usually designated "fatty degeneration" of the cells.

Central necrosis has considerable surgical interest since it occurs in *chloroform poisoning*. Fischler's experiments have shown that the process is by no means simple, but is related in a complicated way to pancreatic activity (19). Ordinarily, chloroform does not injure the livers of healthy animals, but if the liver is short circuited by an Eck fistula, it produces

the typical central necroses very speedily and the animals die in a peculiar comatose condition (20). In animals with Eck fistulæ, similar changes may be produced by poisons other than chloroform but some animals which have had these fistulæ for some time, are not more sensitive to chloroform than normals. Fischler believes, therefore, that chloroform is merely an activator in the production of these changes. A liver injured in some way seems to be hypersensitive to the trypsin derived from the pancreas, for if an animal has been previously immunized to this enzyme, it does not develop a central necrosis, notwithstanding the Eck fistula plus chloroform (Bergmann and Gulecke). The correctness of this view is vouched for clinically by the observed coexistence of central necrosis and pancreatic fat necrosis (Adamski's case (21)), a combination which has also been seen experimentally. According to Fischler, death in central liver necrosis results from a flooding of the circulation with liver substance split by trypsin, and is therefore a death from split protein intoxication. Clinical reports of death after chloroform anesthesia similar to the deaths of liver necrosis or acute yellow atrophy, have been frequently described in the literature (22), but in these cases, the authors failed to take into consideration the possibility of a hypersensitiveness of the liver to chloroform. This peculiarity of patients with icterus is known to every surgeon and for this reason ether is the preferred anesthetic.

[A decisive factor in chloroform necrosis of the liver is the diet. Animals who have been starved are much more susceptible and are injured to a greater degree. Interesting facts have been brought out, not only in this connection but also in the repair of such injuries, by Whipple and his associates. It seems that when the liver is injured by chloroform, the necrosis involves the lobules beginning in the center and extending outward to approximately the same degree throughout the entire organ. If therefore a small section is removed at intervals after poisoning, the process of repair can be followed with great accuracy. The necrotic debris is removed by autolysis and absorption, and new liver tissue then grows in. The rate at which this repair proceeds has been studied, and it was found that complete regeneration can take place in from seven to ten days. During starvation, the rate is slower; a diet of bread and skimmed milk is the best for repair, skeletal muscle is less favorable and so on. The amount of carbohydrate present is the important factor. Fats have no influence.

Two problems of more general interest also have received light from these investigations.

"The protein sparing action" of carbohydrates is well recognized through the efforts of Lusk and others. That is: during fasting, less nitrogen (protein) is lost if the body is well stocked with the carbohydrate

glycogen; the addition of added amounts of carbohydrates to a diet insufficient in proteins will decrease or prevent the loss of nitrogen; and finally, carbohydrates added to a diet already containing nitrogen sufficient to maintain equilibrium will bring about storage of protein. The mechanism of this action is not understood but it is believed by some that it occurs "at the source," *i.e.*, carbohydrates spare proteins by inhibiting the intracellular enzymes which destroy the latter. Others believe that it occurs by way of chemical union between partial oxidation products of carbohydrates such as lactic acid, and the end products of protein catabolism. An actual construction of new tissue takes place from a portion of the carbohydrate molecule.

These experiments on liver regeneration seem to support the latter view. The addition of sugar to the diet of the poisoned animals led to a marked diminution in nitrogen excretion, *i.e.*, the nitrogenous bodies which would have been excreted were captured and combined with the sugar to help form new liver tissue.

The second more general proposition concerns growth. The rate of repair of the liver is so rapid that fully 800 grams of liver grow in seven to nine days. Were a tumor to grow at the rate of 100 to 150 grams per day (about the size of a normal spleen or kidney), the surgeon would no doubt be dumfounded. This great capacity of the liver to repair and grow should offer a remarkable opportunity to study problems of growth in general (23).]

In addition to these various functions, the liver is concerned in *blood coagulation*. The cause of delayed coagulation is either lack of fibrinogen, or an excessive amount of antithrombin in the blood. We know that in experimental destruction of the liver by chloroform (24), phosphorus or other injurious substances, not only is there a lack of fibrinogen in the blood, but also an increase of antithrombin in the liver, a substance which inhibits blood coagulation (25). The latter is found in other organs also, but whether these antithrombins of various organs are identical is not known at present.

It is naturally quite clear that we can interfere but little with our surgical equipment in this complicated metabolism of the liver; in other words, the surgical therapy of diseases of the liver is far from promising. The surgeon's interest is centered especially upon the conditions in which an acute cessation of metabolism swamps the organism with poisonous substances which endanger the benefits of some operation, possibly performed on an entirely different part of the body. Unfortunately, our knowledge in this respect is still fragmentary, but the investigations of death from chloroform have at least shown us in which direction to turn our attention.

Surgical therapy in diseases of the liver confines itself to its *circulatory conditions* and to those of the portions of intestines dependent upon them. We must therefore become acquainted with the experimental investigations of the hepatic circulation (26). In man, and in those animals which differ from the dog in not having extensive anastomoses, the anatomy of which is described especially well in Rio Branco's (27) work, ligation, or embolic occlusion of the hepatic artery is followed by necrosis of large amounts of liver tissue. The numerous experiments on this subject have been compiled by Narath II. Of later investigators, we need mention only Cohnheim and Litten, Janson, Ehrhardt, Haberer, Narath (28).

The results obtained by older authors do not agree in every detail, the reason being that the ligature was not always applied at the same place and many overlooked possible abnormal collateral branches, which are found at times in man, and more often in the ordinary laboratory animals, especially the dog. Haberer (28) with due consideration of all these possible sources of error, conducted a series of investigations by *ligating the hepatic artery* at various places, and immediately after death, following this by injecting the vessels through the aorta. He found that if the artery is ligated before the branching of the gastro-duodenalis, the collaterals are sufficiently numerous, and act promptly enough to prevent changes in the liver. If this collateral circulation is narrowed down by applying a ligature between the gastro-duodenal, and the pyloric arteries, then small necroses are observed, while ligation of the hepatic artery proper leads to total destruction in spite of the arterial blood still flowing through from arteries in the diaphragm, or from possible abnormal hepatic branches.

V. Haberer's, and later Nicoletti's experiments (29) have also shown the effect of ligation of the two end branches of the hepatic artery. Necrosis involves the lobe indicated only when it is comparatively isolated, as is the case in rabbits. According to Nicoletti, the broad junction of the hepatic lobes with each other in man, makes it possible to ligate the final branches of the artery, but Narath (28) and Thole (30), believe the danger of necrosis is too great. As a whole, the results of experimental and anatomical investigations have been confirmed on man in both the cases in which the artery has been ligated by accident or intentionally (aneurysm) as well as in the rare pathological condition of embolism (Chiari) (3), (28). According to Narath II, there are about 20 cases in the literature in which the hepatic artery or separate branches have been ligated operatively. Humans can undoubtedly tolerate ligation of the common hepatic artery; but ligation before the gastric artery branches off, leads to small liver necroses. Ligation near its origin is possible with-



out extensive necrosis, only when there is a well developed collateral circulation such as usually develops after ligation of the main branches (31). Everything depends on the collaterals, but their extent can hardly be estimated beforehand (see Narath). If, however, arteriosclerosis involving the hepatic artery or extensive adhesions are present about the liver, the collateral circulation is usually sufficient, and ligation of the artery near the coeliac axis would be feasible. Bourdenko (32) has utilized this fact in animal experiments by suturing the omentum to the liver thereby obtaining a collateral circulation, and then after some days, tying off the hepatica propria. The results were by no means conclusive, but he believed that the necroses were less extensive. Villandes attempted to avoid the danger by slowly constricting the lumen of the artery before final ligation.

Still another method was devised by Narath II (28) who established an anastomosis between the renal artery and the portal vein by means of a suture and found that his animals lived and showed only minor changes in the liver. He obtained similar results by implanting the severed hepatic artery into the portal vein, which amounted to the same thing. These experiments are intensely interesting from every standpoint. First of all, they show that the liver cells are able to extract the arterial blood necessary for their nutrition from the portal circulation when this contains it. This was demonstrated especially well in one of the dogs in which an embolus obstructed the portal vein to one lobe, which consequently became necrotic, while the other lobes were undamaged. Furthermore, the portal vein and its surrounding connective tissue are not dependent for blood supply on the vasa-vasorum, for even in the absence of these vessels, they do not perish from necrosis. But it is not known whether the vessel wall receives its blood supply from the portal vein itself or from other sources.

Narath II and Steckmacher (33) studied histological changes in the liver after ligation of the hepatic artery. Among the more important findings are periacinar connective tissue proliferation and cyst formation, both described by Janson (28) also. It must be emphasized that this formation of connective tissue following necrosis has nothing in common with true cirrhosis of the liver (see Lissauer (34)).

The changes after sudden *ligation of the main trunk of the portal vein* cannot be studied in animals because death usually takes place after a few hours (35), but in dogs and cats single branches can be ligated without fatal results (36). Ehrhardt stated that in the cat, nutritional disturbances of the liver cells resulted from ligation of the branches of the portal vein supplying them. The normal fat content of the cells oscillated and the blood content of the liver lobules became minimal. In a number, cicatri-

cial shrinking was found after two to three months. After more extensive ligation, the livers showed changes quite similar to cirrhosis. Solowieff (37) had observed this before, after a gradual occlusion of the portal vein, and he was enabled to keep the animals alive for months. Steenhuis also found in his extensive experiments on rabbits that after ligation of separate branches of the portal vein the corresponding lobes were always shrunken, while the others showed a compensatory hypertrophy. Ligation of such isolated branches is not fatal because the portal system is not a closed unit, but anastomoses with branches of the superior and inferior vena cavae, and is in close connection with the hepatic artery also (Josselin de Jong's work discusses these anatomical relations). Changes in the liver in the sense of cirrhosis have by no means been consistently observed after ligation of the portal vein (38) and certainly not after its partial elimination as was undertaken by Cohnheim and Litten and others (39). They occluded the large vessels by introducing globules of wax into the portal vein, but found no alterations in the liver. On the other hand, Zahn (40) who used mercury for emboli, observed so called "red infarcts" which means foci of atrophy of liver cells with capillary dilatation. Chiari (41) points out that the type of liver change under these conditions depends on whether the involvement includes the interlobular branches or is only in the larger trunks. In the latter case, the interlobular anastomoses with the hepatic artery remain intact, and these inner "portal vein roots" supply a large amount of the blood otherwise excluded.

The results of these experiments are in perfect harmony with the changes following portal vein thrombosis (42). Of course, here too the secondary anastomoses formed by the portal vein play an important part. The esophageal and gastric veins dilate as do those of the abdominal wall (caput medusæ), and a quickly fatal hemorrhage may result from rupture of these esophageal varices. Furthermore actual cavernous dilatation of the veins of the hepatoduodenal ligament has been observed and total obstruction of the portal vein may finally be compensated, thus prolonging the life of the patient (43).

If, therefore, ligation of a branch of the portal vein is permissible and compatible with life, nevertheless, "the ligation of the main trunk of the portal vein generally kills the patient," as Langenbuch (44) expresses it.

What is the *cause of death in total occlusion of the portal vein* in man or animals? Numerous investigative results are available, for ligation of this vein is a particularly suitable method for studying the physiology of the liver; although the animals do not live for more than a few hours. Death is generally supposed to result from exsanguination into the enteric vessels, but yet they cannot hold enough to cause death from hemorrhage as

Tappeiner (35) points out, and Ehrhardt (36) has shown that no such remarkable stasis really occurs.

Tappeiner carefully investigated blood pressure, rapidity of outflow, pulse, etc. during exsanguination, and also after ligation of the portal vein, but was not able to explain why "the blood is placed in such a condition that it cannot participate actively in the circulation" after portal obstruction ((35) p. 64).

According to investigations of Thole (6), a notable depression of blood pressure occurs after experimental ligation of the portal vein with intact vagus, and the animals die in collapse. If the vagi are cut, these symptoms develop more slowly, so that an infarct of the intestines appears. To sum up: We may say that death after ligation of the portal vein results either from collapse, or from intestinal congestion (infarction). Thus far, the cause of this collapse is unknown.

That elimination of liver function is not the cause of death is obvious, since death results so quickly, and since the numerous experiments with Eck's fistulæ (45) have shown that mere short circuiting of the liver is a procedure entirely compatible with the life of an animal or man (see case of Rosenstein (46)). We cannot discuss here the changes in metabolism which follow Eck fistulæ. A question of possible future surgical importance is still debated, *viz.*, whether animals with Eck fistulæ may be permitted a meat diet, and on what the severe collapse, occasionally observed after such a diet, depends. The surgeon is interested in the Eck fistula chiefly because it relieves the peripheral stasis incident to portal obstruction. We shall return to this in discussing ascites and its therapy. Furthermore, after establishing an Eck fistula, the whole liver may be extirpated in animals, but they live only a few hours (38).

Experimental *obstruction of the hepatic veins* has often been used to study retrograde embolism (47). Arnold observed a very instructive case of this condition and made it the starting point of experimental investigations which showed that obstruction of the hepatic veins results in the appearance of red spots in the liver corresponding to engorged capillaries. In a number of clinical cases of thrombosis there were found nodular hyperplastic foci, capsular thickenings, increase of connective tissue along the hepatic vein which was tortuous, and degeneration of the parenchyma (48).

It is interesting to note the reaction of the liver to temporary pinching off of vessels, especially those in the hepatoduodenal ligament. Its corollary—how the lesion resulting from this cause or from obstruction or stasis can be counteracted—is also of interest.

To check hemorrhage during resection of portions of the liver the most rational method is, of course, *temporary compression of the hepatoduodenal*

*ligament*, and this has been done repeatedly both experimentally and in man (49). Opinions as to the results differ. Some state that its compression for as long as one hour does not cause observable lesions, while others consider this method of temporary hemostasis impossible, because, as stated above, rapid collapse and death followed either this procedure or ligation of the portal vein (Langenbuch). Ransohoff (50) also points out that a fall in blood pressure is caused by merely inserting a finger into the foramen of Winslow, while Burdenko observed chromatolysis in the abdominal ganglia.

With these contradictory statements, it is probable that the differences lie not so much in erroneous observations, as in individual variations in the animals and in the nature of the experiments. Thoele emphasizes that in man, the portal vein can be occluded for only a short time and then only after the arterial supply has also been closed off. Perhaps the differences in results depend on the simultaneous obstruction of both artery and vein.

The most important, and for the patient the most distressing, result of stasis in the portal circulation is *ascites* (51). Its development, as well as that of edema is often considered due to mechanical causes, assuming that the fluid passes out of blood vessels somewhat like a creek overflowing its banks when its natural outlet is dammed; *i.e.*, it is purely a result of obstruction. The fact is, however, that ascites may be due to various causes, which according to Quinke, may be grouped as follows (52) :

I. Increase of inflow.

- (a) Increased inflow of lymph.
- (b) Increased secretory activity of the endothelium.
- (c) Increased permeability of blood vessel walls from congestion or inflammation. (In the latter, probably the altered activity of the endothelium is an important factor.)

II. Decreased outflow.

- (a) From obstruction to efferent lymphatics.
- (b) From decreased absorptive power of endothelium.
- (c) From decreased absorptive power of the blood vessels, *e.g.*, in passive congestion.

Naturally this classification has only didactic value. As Quinke himself remarks, in some cases several of these factors are present or follow each other. But the ascites due to congestion is still differentiated from an inflammatory exudate by the greater albumen content and the more numerous leucocytes of the latter. But quantitative determinations show that such a comparison is not always possible because middle



values are found so frequently. Furthermore, in many cases there is an uninterrupted course of events from transudate to exudate. Pure obstructive ascites, in the old sense of the term, can hardly be said to exist (53). For the development of any ascites there is required a disturbance in the intermediary water and mineral metabolism of the cells, chiefly perhaps the endothelium, but a disturbance which must be classed under the group of "inflammations." According to our present opinion, the overflow of fluid is not a simple leaking of serum through a more permeable vessel wall, but is a result of a specific activity: a "secretion" of the endothelium. Theoretically, therefore, it is not justifiable to draw a sharp distinction between obstructive and inflammatory ascites, since the difference between the two is one, not of kind, but of degree.

But for practical purposes, the differentiation is highly important. An exudate ordinarily indicates a bacterial process, whether it be due to primary bacterial action, to infection from careless puncture, or to infection of a transudate which on account of its long duration has rendered the intestinal wall more permeable to bacteria (54). Even though we may be able to determine in a general way that an exudate is due to bacterial processes, the actual factor which causes the inflammation and disturbs cellular metabolism so that fluid is poured out, remains unknown. Only when this is recognized, will we be in a position to understand the reasons for the frequent failure of our therapeutic measures, which in the main, attempt to improve the circulation. The question of whether or not this disturbing factor resides simply in the congestion itself, can perhaps be answered by experimental obstruction to the portal circulation.

The very careful investigations of Ito and Omi (55) who obstructed the portal circulation gradually, have demonstrated that no ascites is developed in animals in spite of marked congestion. The clinical findings in slowly developing portal thrombosis are of less deductive value on account of the varied etiology (56), (42). The frequently cited case of Langenbuch in which ascites developed after numerous small branches of the portal vein were ligated during resection of a lobe of the liver, is not clear cut because as the author himself states, it was complicated by erysipelas. In a number of instances on record, portal thrombosis was associated with ascites, in others, such was not the case (53). On the other hand, not a few cases of cirrhosis of the liver show ascites when no trace of stasis in the portal circulation can be discovered at autopsy. The splenic tumor in cirrhosis of the liver is not due to congestion, but is inflammatory. It follows that we must be very careful in interpreting the importance of congestion in ascites, especially that following cirrhosis of the liver, and we must not be too optimistic in expecting a cure of the ascites by operative improvement of the abdominal circulatory conditions (38).

The most common operation for this purpose is that of Talma and Drumond (57). These two surgeons, from anatomical considerations, simultaneously and independently proposed that a free anastomosis be established from the portal vein to the inferior vena cava by fixing the omentum, spleen, liver and gall bladder to the anterior abdominal wall. We know that in cirrhosis of the liver the natural communications between the portal vein and inferior vena cava are often much distended, leading among other things to the dangerous varices of the esophagus, or to the classical *caput medusæ*. Experimental investigations were made of the possibility of eliminating the liver after omental fixation, *i.e.*, to determine whether sufficient anastomoses would develop. Tillmann (58) ligated the portal vein after one of these operations in a dog, without important damage. But this well known experiment failed to answer its original question because at autopsy, not only was the portal vein only partially obstructed, but there were numerous collaterals in this area. Furthermore, many workers who did not suture the omentum to the anterior belly wall succeeded in gradually ligating the portal vein in dogs without fatalities (59). On the basis of their investigations, Ito and Omi assume that the last mentioned writers unintentionally produced a peritonitis, which led to broad anastomoses between the abdominal organs and which may explain why the dogs escaped the consequences of their operations.

Moreover, their experiments show that omental fixation does not always suffice to prevent death, and only the formation of broad adhesions of the abdominal viscera to the anterior abdominal wall and to each other, insures the development of sufficient collaterals. For this reason they suggest treating the ascites of cirrhosis by producing such adhesions. Referring to what has been said above regarding the cause of ascites in cirrhosis, it appears somewhat doubtful whether this quite dangerous method would be better than simple omental fixation. The same may be said in regard to establishing an Eck fistula, a method which has been used but seldom in man. At any rate, Rosenstein's patient who survived the operation for some time was not entirely relieved of the ascites by this procedure (60). Detailed statistics of the operative results in about 300 cases of the Talma operation are furnished by Bunge (61). He showed that ascites disappeared in only 30 per cent. Later figures appear to be somewhat more encouraging (see Hopfner (51)).

The unsuccessful results of the various operations show with almost the certainty of an experiment, that stasis is not the only cause of ascites, although it must be admitted that it is a real and essential factor in the appearance of a transudate in cirrhosis of the liver. The practically harmless Talma operation therefore seems justifiable. In passing, it may be mentioned that Talma himself did not consider the ascites in cirrhosis the

result of congestion alone. Up to the present, attempts to establish more clear cut and definite indications for Talma's operation on the basis of hepatic functional tests, have failed and will continue to fail, for the simple reason that neither the place nor the mode of action of stasis is known.

In the few instances of sudden death following Talma's operation, Kretz attributed the fatal outcome to a sudden flooding of the circulation with substances which otherwise would have been detoxified in the liver. These deaths must, therefore, be considered analogous to those observed occasionally in Eck-fistula dogs (see above).

In contrast to these procedures which combat ascites by improving stasis, are those which confine themselves to symptomatic treatment and remove the fluid by early and frequent puncture (Ewald (62) a.o.), or by permanent drainage. To make the latter possible, the saphenous vein with its opening into the femoral vein intact, is turned upwards and introduced as a drain into the abdominal cavity (Rouotte's operation (63)), or silk threads, or silver wire (64) carried from the abdominal cavity into the subcutaneous tissues have been used to induce the growth of new lymph vessels (for other methods see Enderlen, Hotz, and Magnus-Alsleben (42)).

In the cure of ascites by puncture or drainage, that is, without new blood vessel anastomoses, a number of factors must be considered (52). By paracentesis, substances are removed which are injurious and irritating to the serosa and which hinder absorption. The mechanical absorptive conditions are improved, the endothelium of the serosa is again placed under physiological conditions, and changes favoring a cure are promoted. In fact, ascites has been permanently relieved in certain instances by this means, and the importance of this form of drainage must not be underestimated. Physiologically, it is at least as logical as Talma's operation, and it is quite possible that the latter influences ascites not only because it relieves the assumed venous congestion, but also because it opens new connections between the lymphatics of the abdomen and the subcutaneous tissue, or in other words, it establishes permanent drainage. But after all, we know very little of the activity of the lymph channels in the formation or the removal of ascitic fluid, although we do know that irrespective of the therapeusis of its underlying cause, the removal of fluid is desirable, because the increase of intraabdominal pressure leads to circulatory disturbances. This will be considered more carefully in the section on ileus.

A most interesting function of the liver is its *bile formation and secretion* (65). As it appears in the intestine, bile is a product of liver cells and of the epithelium of the bile channels, especially the gall bladder. It is delivered from the liver as a thin watery fluid; its peculiar viscid

consistency is due to the mucin secreted by the epithelium of the bile channels (66). But the consistency of bile changes not only with its mucin content but with its content of water. The chief constituents are the bile acids, which are conjugation products of cholic acid and glycochol or taurin (glycocholic acid and taurocholic acid), and bile pigments.

For the other chemical substances found in the bile, the reader is referred to Wohlgemuth (67). The numerous investigations of the source of bile acids and bile pigments have now quite definitely established the fact that the acids originate mainly, if not exclusively, in the liver itself. A question of great importance in the etiology of gall stones is the source of the cholesterin found in the gall bladder. Since the bile of that structure contains more cholesterin than liver bile, Naunyn (68) assumed that it was a product of the gall bladder epithelium, but Aschoff (69) believes that it comes chiefly from the liver.

In addition to these normal constituents, the bile also eliminates substances which have been ingested as medicines. We cannot discuss the details here (38). This is the basis of all efforts to dissolve gall stones by medicines, or to disinfect the bile channels (70).

*The formation of bile*, as Barbera (71) attempted to prove in numerous investigations, is a result of the metabolism of the liver cells. The color and the chemical composition depend to a certain extent on the blood supply. At least, Colasanti (cited by Wohlgemuth) observed a colorless bile, very poor in bile acids in a gall bladder fistula dog, whose portal vein had been ligated. In the literature, a certain prominence is given to cases in which a nearly colorless bile is secreted, *i.e.*, acholic stools without icterus. They are usually associated with extensive changes in the liver, such as tuberculosis or very advanced fatty degeneration and infiltration (72). Thus far, total failure to secrete bile has not been observed with certainty (73). Leukourubin formation, in which the usual hydrobilirubin has been further reduced in the intestine, as well as fatty and milk stools, are often mistaken for acholia. Nor must the colorless bile found in degeneration of the liver cells be mistaken for the white bile found in hydrops of the gall bladder (see later).

The quantity of bile secreted varies within wide limits, and observations made on man or animals with gall bladder fistulæ, can be utilized only with caution. It is true that both man and the dog tolerate the complete absence of bile from the intestines comparatively well. Mayo Robson (74), for instance, was enabled to observe and experiment for 15 months on a patient with a complete gall bladder fistula. Nevertheless this continuous and total loss of bile can scarcely be considered a matter of indifference to the general metabolism. Recent observations, especially of severe osteoporosis with gall bladder fistulæ have taught us better.



The statements of the quantity of bile flowing from biliary fistulae must not be taken too literally, because the amount excreted may in reality be larger, or it may be less. Brand (75) compiled tables of the quantity secreted by different individuals in 24 hours, according to different authors. He gives figures ranging from 16 c.c. to 1122 c.c. Mayo Robson observed from 860 to 1133 c.c. in his patient.

The liver, of course, secretes constantly, but in varying amounts. The daily curve of secretion usually begins to rise during the early morning and reaches one or two maxima during midday and evening hours, followed by a fall during the night until the early morning. The curve may be explained by the taking of food which undoubtedly influences bile formation. In the details, the statements of the various workers are very conflicting; but it may be gathered that water has no influence, while a protein diet increases bile secretion (76). In regard to fats and carbohydrates, opinions are hopelessly contradictory. While some observed considerable increase after fat feeding (77), others found a decrease (Mandelstamm, Thomas, Stadelmann); clear proof that the much used method of the gall bladder fistula is very unreliable.

From the investigations of Stadelmann and his followers which were made with every conceivable precaution, it can be stated that the increase in bile secretion observed after protein diet is seen only when compared to that in the same animal during starvation, and that immediate increase of bile formation after feeding is not consistently observed.

Of the chemicals credited with bile stimulating action, very few have survived critical tests. The bile acid salts are of special interest because, according to the consensus of opinion, they always induce an increased bile secretion and are probably important in the physiological process (78). These salts are absorbed in the upper intestine, reach the liver through the blood, and then are re-excreted into the intestine with the bile, a process often designated as "the biliary circulation." Furthermore biliary secretion, according to Asher (79) and his pupils, is stimulated by the direct action of albumoses and peptones on the liver cells, but the secretin of the small intestine has very little, if any, such powers (see under pancreas (80)).

The quantity depends moreover on the amount of blood which flows through the liver. Consequently, ligation, especially of the hepatic artery, leads to a change in secretion. It follows that the tonus of the blood vessels of the liver will have a modifying effect. But inasmuch as the hepatic artery and the portal vein have a contrary innervation, *i.e.*, arterial vaso-constrictors travel with the vagus, and dilatators with the splanchnics, while in the portal vein the reverse is the case, it must be

assumed that the vessel tonus is more or less balanced (67). Rost, however, observed in animals that psychical stimuli influence bile formation, but the effect is not as marked as in the stomach. This is no doubt due to the absence of true secretory nerves in the liver.

Bile from the liver cells is not discharged uninterruptedly into the intestine under normal conditions. As may be observed at any time in dogs with duodenal fistulæ, all the digestive glands rest during starvation, and only a few drops of a grayish brown, alkaline intestinal juice are discharged. But this quiescence is interrupted about every hour, when the so-called "emptying action" of all glands occurs and they secrete for about 10 minutes, during which time the gall bladder also discharges several cubic centimeters of bile, in two or three single jets (81). Apart from this, food as it passes through the duodenum causes contraction of the gall bladder, and opening of the sphincter of the papilla of Vater (82). Since Pawlow's investigations, it is known that albumoses especially, *i.e.*, protein derivatives, lead to this flow of bile. Hydrochloric acid may also be effective, but pure fat does not stimulate the flow, nor does pure sodium oleate (Rost). When fat has been split, however, either by the action of other digestive secretions, or by long standing (rancid), an abundant flow results; although it is not known what particular substances formed in this chemical process are the stimulants (83). For practical work in nutrition, it is important to know that fat given by the mouth is split up sufficiently to stimulate a profuse flow.

We are dealing with an extraordinarily delicate reflex mechanism when we experiment with the nerves which regulate the *movements of the gall bladder*, bile ducts and the musculature of the papilla of Vater. Doyon (84) supported by his experiments, stated that the splanchnics are the motor nerves of the bile passages, and, furthermore, that stimulation of the central stump of the vagus is followed by dilatation of the sphincter of the papilla of Vater and synchronous contraction of the gall bladder. Bainbridge and Dale (85), also Courtade and Guyon (86) in a later work, came to somewhat different conclusions for they found that stimulation of the splanchnics caused relaxation of the gall bladder, while stimulation of the vagus caused its contraction, with simultaneous opening of the papilla of Vater. It is not as yet known what part is played by the nerve plexuses in the gall bladder, and by the ganglia distributed throughout the bile channels. Their anatomical structure can be found described by Dogiel (87), who also made pressure calculations on the gall bladder. Reach (88) devised a method of studying the living bile passages and noted the influence of poisons on their motor conditions.

The *functional importance of bile in digestion* has been frequently underestimated (89). In the first place, it is certain that the bile helps

in fat absorption, and in its absence, only from one-seventh to one-half of the normal quantity is taken up (90), and yet the well known observation of Claude Bernard (91) showed that bile without pancreatic juice does not permit fat absorption. He found in rabbits, in which the entrance of the choledochus is higher than that of the pancreatic duct, that no fat is demonstrable in the chylus ducts between those two openings, but below the pancreatic duct the papillary lymph vessels are milky white and opaque. Dastres (92) experiment, on the other hand, proves that pancreatic juice alone does not emulsify fats, for after ligation of the common duct he produced a cholecysto-jejunal fistula and found the chyle ducts filled with fat only below the entrance of this fistula. It seems that the filling of chyle ducts with fat is brought about by a specific stimulation which bile and pancreatic secretion exert on the papilla of the intestines (93). That the fat splitting property of the pancreatic juice is intensified by the presence of bile acid salts in the bile, and that artificially prepared bile acid salts have the same property, is shown in the investigations of Rachford and Magnus (94).

Exclusion of bile from the intestine leads to decomposition of the feces from this failure in fat absorption. For this reason, it was supposed that the bile was an antiseptic, but since the discovery that even in complete absence of bile, fecal decomposition does not take place on protein and carbohydrate diets, this idea was abandoned. This finding, however, has not been uniform among various workers (66). Bile is also active in protein digestion in checking the activity of pepsin. As Hammarsten (95) first demonstrated, and it can be easily verified in dogs with duodenal fistulæ, bile forms a precipitate taking pepsin with it in the presence of an acid gastric content rich in proteins. On the other hand, it increases the protein digestive power of the pancreatic juice (96), so that it is not surprising that Rosenberg (77) found no change in the utilization of the nutritive substances when maximal quantities of proteins were given before and after establishing a complete gall bladder fistula. The amylolytic power of pancreatic juice is also supposedly increased, but the bile is said to contain a starch splitting enzyme (97).

The salts of bile acids are used as cathartics because of their mild though effective action and in mentioning this influence of bile in stimulating peristalsis, we have completed, in rough outline, the picture of the physiological activities of this secretion (98). This review has shown that bile is a very essential factor in the digestive processes, and if Mayo Robson's patient with her total gall bladder fistula remained in good health for 15 months, it only "proves that the animal organism in some manner always finds ways and means to replace lost functions" (99).

Of all effects resulting from disturbances in the flow of bile, the most important and striking is *icterus* (100). Jaundice develops when bile cannot flow into the intestine because the ducts are obstructed. There is first a stasis in the bile channels, which results in rupture of the intracellular bile capillaries, as demonstrated by Eppinger (101), and then, according to Fleischl's investigations (102) the bile passes either through the lymph channels of the liver into the thoracic duct and enters the blood by this route, or passes directly into the blood capillaries (103). In such cases of mechanical obstructions, as, for example, by calculus in the common duct, or from compression by a carcinoma, the stool is clay colored from the absence of bile pigments. Theoretically, the gall bladder should be distended, but in cases in which it is shrunk from previous inflammatory processes, at the time of occlusion, it cannot distend as it would in ordinary chronic calculus disease. On the other hand, with tumors in the pancreatic region or at the papilla, the gall bladder is usually normal, and consequently, on occlusion of the bile duct, it distends considerably. This Courvoisier's sign (104) is important in differential diagnosis. With such a complete occlusion of the common duct, no urobilin or urobilinogen is found in the bile, which is correlated with the "biliary circulation," mentioned previously (38).

[The question of how much of the duct system must be obstructed before clinical jaundice appears is interesting for several reasons. There is apparently no data available for the human subject, but McMaster and Rous have determined that the ducts from three-quarters of the liver substance in dogs and monkeys can be obstructed without pigment or cholate accumulation and that tissue icterus did not result when nineteen-twentieths of the liver substance was placed in stasis (105).]

This mechanical form of icterus, easily understood physiologically, has always been distinguished from the so-called hemolytic or toxemic icterus, the distinction having been first made from the clinical observation that there are cases of icterus in which the feces remain bile stained. This condition, of course, does not follow simple stasis from obstruction of the larger bile channels. The common factor in the diseases leading to this form of jaundice is a destruction of erythrocytes which liberate hemoglobin. It was formerly thought that the liver was not concerned in this hemolytic icterus, especially because, in other places in the body, as for example, the subcutaneous connective tissues, extravasated blood is changed into hematoidin, which is chemically an isomer to the bilirubin of the bile (black and blue marks). But the error of this theory was shown by Minkowski and Naunyn (106) who poisoned geese and ducks with the strongly hemolytic arsine and did not obtain icterus if the liver had previously been extirpated. Recently, McNee (107) repeated and amplified



these investigations, and on the strength of his histological findings, reached the conclusion that it is not the liver cells but the endothelium of the liver capillaries (Kupfer's star cells) which is concerned to a large degree in the formation of icterus. Since similar endothelial cells are present in the spleen and bone marrow, and the iron free moiety of hemoglobin can be split off there, he considers it quite possible theoretically, that the endothelium of these organs also plays an essential part in this type of icterus. Observations along similar lines have been made by the determination of the bilirubin in the splenic blood in which it was found that this blood contained more than blood taken from the finger tip (108). But these investigations are all only beginnings and great care should be exercised in their interpretation (see Fischler's (1) critique of the experiments).

As a consequence of the increased blood destruction, the bile becomes much thickened and especially rich in pigments, so that the ducts cannot be emptied by the usual secretory pressure of the liver (100). The bile is thus dammed back, forced into the lymphatic system, and icterus results. This theory which thus classes hematogenous icterus with stasis, was supported by the demonstration that, as in stasis icterus, the bile channels rupture and thus directly cause icterus because bile capillaries are plugged with so-called bile thrombi (108). On the other hand, since this process is not clearly understood but is a consequence of blood changes, the differentiation of hematogenous and obstructive jaundice is perfectly valid, although the mechanism of the former is not as was formerly supposed, but approximates that of obstructive icterus. Finally, Kretz (109) points out that by the destruction of liver cells, communications are opened between bile capillaries and the smallest lymph vessels and this would probably lead to icterus. Whether alterations in the liver cells are responsible for certain still obscure forms (catarrhal, familial, neonatorum) by diverting the bile from its normal course, has not yet been established, although the indications seem to point in that direction (compare later in regard to hydrops of the biliary system).

The *blood changes which lead to hematogenous icterus* are of a most varied nature, but as far as is known, they all have the one thing in common, *viz.*, the escape of hemoglobin from the erythrocytes. This may be brought about by specific blood poisons such as arsine or toluenediamin; by those which form methemoglobin, potassium chloride and pyrogallol; and by a large group of blood diseases classified under the name of pernicious anemia. These latter diseases are closely related to splenic pathology and will be discussed in that chapter (110).

The cases of *icterus associated with hematomata* are especially interesting to the surgeon. Their mutual relationship is not clear, since the combina-

tion is more or less rare, and consequently has not been systematically studied.

*Toxic jaundice* may also be referable to mechanical occlusion of the biliary capillaries by thrombi, and possibly to swelling of the liver cells.

The *results of icterus* are first noticeable in the liver itself (lit. by Quinke (52), p. 57). In obstructive jaundice, *i.e.*, stone in the common duct, there is distention of all the bile passages; in fact, cases have been observed in which approximately one liter of bile had accumulated in them. The liver cells continue to secrete for some time, but they are soon injured both by the mechanical pressure and by the chemical action of the bile. Glycogen accumulation, as well as the excretion of bile acids decreases, and later, the simplest morphological observation will show that a severe cell injury has occurred. In place of the destroyed parenchyma, connective tissue grows in, the bile ducts proliferate, and as Nasse showed in animals, the liver becomes shrunken and atrophic.

These morphological changes have been frequently studied in animals and although the different species showed but slight variations in the final pathological findings, it was found that some animals tolerated the ligation of bile ducts better than others (111). Icterus appears in three days after duct ligation, but if the thoracic duct also is tied off, the appearance of tissue icterus is delayed for weeks (112). Jaundice develops promptly, of course, if the bile is conducted directly from the gall bladder into the blood through a fistula into the vena cava, as was performed by Burger and Fischer (113). The changes in the liver are further complicated by adventitious infection, which is favored by the stagnation of bile. The importance of infection in the appearance of the histological changes described is doubtless great, because Frey and Harley (112) after ligating the common duct under aseptic conditions, did not find the foci of round cell, nor the cell necrosis, described by Cohnheim and Beloussow, but they did develop when peritonitis was superimposed (111).

When bile enters the general circulation, the injury is not confined to the liver alone, but the entire organism feels its effects. The toxic process may be very complex and it seems to be due in large measure to cholic acid which irritates the central end of the vagus with resulting slowing of heart action, and later, paralysis of some of the medullary nuclei (114). But to what extent the cerebral phenomena—depression, delirium convulsions, etc.—depend on the same substance is not known. Hepatic insufficiency may be an underlying factor, or it may be the bile substances, especially pigments, to which suspicion has lately been turned (115).

Morawitz and Bierich (116) investigated the *delay* in the *coagulation time* of the blood in jaundice, and found that the bile acid salts are

not at fault, because even in the most severe cases, the blood does not contain sufficient cholates to account for the delay. Furthermore, it is not proportional to the depth of the jaundice. Clinically, it is remarkable that not every jaundice leads to this decreased coagulability, and hence to those most disagreeable postoperative secondary hemorrhages. The impression is gained that catarrhal icterus is more prone to hemorrhage than the icterus following calculus in the common duct.

A diminished fibrin content could not be demonstrated. Experiments were so devised that a properly chosen dose of hirudin was added to various samples of blood, to produce a great delay in the coagulation time of the sample from an icteric patient who bled freely, but not sufficient to cause change either in normal blood, or in blood from icteric patients who did not bleed freely. The deduction was made that the decreased coagulation of the blood is due to a delayed formation of the fibrin enzyme, probably on account of a deficiency of thrombokinase, but the reason is not clear. Kunika's (117) opinion, that icterus is accompanied by absorption of substances liberated in the destruction of liver cells, is but an unproved hypothesis.

The combination of *anuria and jaundice* is a peculiar one, their physiological relationship has not been determined (118). In eight out of thirteen dogs, there occurred a delayed elimination of indigo carmine and phlorizin sugar after ligation of the common duct, and renal injuries, similar perhaps to those in patients with anuria, were present.

*Gall stones* are the most frequent cause of mechanical obstruction to the flow of bile. Modern knowledge of cholelithiasis begins with the work of V. Helmsbach (119) who drew an analogy between the calculi found in man, and pearl and shell formation in molluscs, by stating that an organic scaffolding was formed by some substance, perhaps from an inflammatory process, to which inorganic salts adhered, causing practically a petrification of the organic base structure. The actual form of the stone would be decided by its position and the pressures to which it was subjected. Naunyn (68) has elaborated this conception, and believes that gall stones form from the precipitation of substances which are normally contained in the bile, especially cholesterol, bilirubin and lime, and that the precipitation of these bodies is primarily due to gall bladder infection, *i.e.*, a calculus forming catarrh.

The formation of calculi in the gall bladder, and in other parts of the body as well, presents a very interesting problem in colloid chemistry (Schade (120)).

Calculi may develop in layers or strata. This presupposes colloidal precipitates such as fibrin, and other proteins which enter the bile in inflammatory processes. With these colloids, crystalloids are precipi-

tated. The architecture of the calculus is therefore stratified at first; later, through secondary rearrangement, especially due to crystalloids a radiating appearance develops. This type is usually represented in the common bilirubin lime calculi of the gall bladder, but urinary, salivary, pancreatic, and intestinal calculi are formed in a similar manner. All originate from an inflammatory process.

Recently the pure cholesterol calculi have been contrasted with the inflammatory calculi, especially by Aschoff-Bacmeister (121), Schade and others, for Aschoff (122), approaching the subject histologically, found no inflammatory changes, either past or present, in a gall bladder which contained cholesterol calculi; but with calculi of the other type, such changes were always present. He concluded, therefore, that calculi could be formed simply by "slow precipitation" of cholesterol without bacterial cooperation, *i.e.*, inflammation. Furthermore, on the basis of animal experiments, and observations with fresh gall bladders, he could not subscribe to Naunyn's opinion that cholesterol is a product of the gall bladder epithelium, merely because these cells contain a larger amount than the liver cells (122). He believed that this may be due to absorption. According to the same writer, stasis alone from mechanical factors such as lacing, pregnancy, etc. is sufficient to encourage the formation of cholesterol calculi. According to Hofbauer (123) the movements of the diaphragm influence the emptying of the bile, and he thinks that the upright position of man, with its diminished diaphragmatic movement, is favorable to gall stones. For this reason gall stones would be exceedingly rare in quadrupeds.

Bacmeister actually obtained this cholesterol precipitation in the test tube, if bile was kept for about a month under sterile conditions. But there must first be some change in the bile before this takes place, and the process was markedly hastened if gall bladder epithelium was added. By combination of the positively charged protein ions with the negatively charged cholesterol particles, the precipitation occurs (124). The details of the colloid chemical conditions in this process are still matters of controversy. Schade (120) assumes that separation takes place when the solvent action of bile in cholesterol is altered, as is the case if the cholate disappears in stasis, and Exner and Heyrowsky (125) have demonstrated that this actually occurs in the autolysis of stagnant bile. They also found less cholate than normal in the bile from the fistula of a gall stone patient.

On the other hand, in certain diseases such as arteriosclerosis (126), diabetes, during pregnancy (127), and in excessive protein intake, there is an increase of cholesterol in the blood and bile. But from a theoretical colloid chemical viewpoint, it is improbable that, unless it be very great,



this increase would lead to marked cholesterin precipitation. It is interesting that such single calculi are frequently found after pregnancy. Chalatoff (128) succeeded in obtaining precipitation experimentally in the gall bladder bile of rabbits by cholesterin feeding, and Verse (129) obtained a marked lipemia with cholesterin deposits in the cornea of rabbits after feeding them with cholesterin and oil.

These demonstrations doubtless support the theoretical possibility that this type of calculus might form by autolysis in sterile stagnant bile, but the question still remains whether the results obtained in vitro apply to the conditions as they occur in man.

According to Kretz (130) the older conception, that these calculi are the product of metamorphosis, still holds good, and on the basis of personal investigations, this theory is supported by Boysen (131); while Aschoff and Bacmeister defend the teaching of their aseptic origin (132), (130).

Kuru (133) believes he could always find fibrin in cholesterin calculi by means of Weigert's stain, and Kretz regarded this discovery as very good evidence for their inflammatory origin. At the instigation of Aschoff, Aoyama (134) reinvestigated Kuru's problem, and also found small amounts of protein scaffolding in the so-called crystallization centers of some true cholesterin calculi, while in others it was absent. In all pigment lime calculi, the protein scaffolding was very dense and easily demonstrable. Aschoff (132), however, pointed out that the value of Weigert's stain in this problem is, to say the least, dubious. In agreement with other investigators, he accepts the theory of inflammatory origin for cholesterin pigment calculi. But he believes the pure cholesterin calculi may be formed under aseptic conditions and that the irritation from these stones may readily lead to a secondary inflammation of the gall bladder.

There is no doubt of the practical value of this differentiation, irrespective of the position assumed towards their origin. Clinically, it is not at all unusual to find gall stone colic with a cholesterin calculus occluding the cystic duct, unaccompanied by inflammation of the gall bladder or infection of its contents. Usually this is seen in the condition known as hydrops (see later) in which severe inflammation is seldom found, in spite of an enormously swollen gall bladder of dangerous appearance, so that we may safely await developments, and operate only if the attack is repeated. It cannot be reiterated too often that an operation is not undertaken on account of gall stones, but because of inflammation in the bile passages. Furthermore, the emphasis laid by Aschoff on the role which the cholesterin diathesis plays in gall stone formation, clears up many questions in gall stone pathology, as, for example, why they are much more frequent in women than in men.

According to the consensus of opinion, they form only in the gall bladder or in the large bile ducts, but after removal of the gall bladder, calculous deposits may occasionally arise in the common duct. Recently, Aufrecht (135) reported, on the basis of certain findings in the stools and in the bile ducts, that the first impulse to gall stone formation is actually given in the liver cells themselves. A practical, and much investigated question is whether gall stones can be dissolved within the gall bladder. v. Hansemann (136) introduced human gall stones into the gall bladder of dogs and was able to demonstrate dissolving effects similar to those observed on sectioning human gall stones. But Aoyama (Aschoff (132)) proved that the gall stones of man, although insoluble in human bile, dissolve in dog bile, which, according to McNee, is related to the fact that the bile of dogs, rabbits and cattle contains in comparison, very small quantities of cholesterin. The diet has a pronounced influence on the absorption of gall stones (137), in glyccol feeding, the calculus diminishes very slowly, but after cystin ingestion it disappears quickly.

As already emphasized, the danger in gall stone disease consists not so much in the calculi themselves, as in the *inflammation* they induce *in the ducts*. In spite of the sphincter of Oddi, it is easy for intestinal bacteria to enter the bile ducts; that the muscle does not always close the opening completely, is illustrated by the fact that ascarides frequently find their way up to the liver. Bacteria which have once entered the bile passages are apt to remain alive and virulent for a long time, for bile is a good culture medium for all sorts of organisms. Indeed, Conradi (138) not only recommended its use for laboratory purposes, but even assumed that the bile more or less neutralizes the bactericidal action of serum, and permits unrestricted growth of the bacteria. Of course, it is not a suitable pabulum for all types of bacteria (139); pneumococci thrive poorly, but all sorts of intestinal bacteria grow very well, especially colon (140) and typhoid bacilli (141). In fact the organisms have been isolated and cultured from the gall bladder many years (decades) after recovery from typhoid fever (142). But organisms suspended in the bile, do not stir up an inflammation of the gall bladder, except when bile stasis (143) or circulatory disturbances are superimposed (144). The degree of inflammation varies, but among many cases, especially of typhoid cholecystitis, are numbers which clinically give the impression of a very acute disease, but no marked alteration is found in the gall bladder wall, although the organ is fuller than normal, probably on account of swelling of the mucosa of the cystic duct.

[For a discussion of the literature and valuable contributions on the mode of infection of the gall bladder, see MYERS, H. F., *et al.*, *Journ. Infect. Diseases*, 1921, 28, p. 456.]

In addition to infection by way of the bile channels, anhematogenous infection of the liver may occur chiefly by way of the portal vein. For this reason liver abscesses are particularly common in tropical dysentery (145), and in suppurative appendicitis.

[In the experience at the Lankenau Hospital, they are particularly prone to follow an appendicitis which involves the mesoappendix, especially when the latter is gangrenous.]

In such cases when rigor indicates the embolic transport of pus, ligation of the right colic, the vein which comes from the appendix, has been suggested (146). The subject of hepatic abscesses from retrograde extension has been discussed by Reiniger (147).

The *surgical procedure undertaken in gall stone disease* consists either in removal of the gall bladder, or in opening it and establishing drainage by means of a fistula. The latter is only a temporary affair, but if drainage of bile to the outside is allowed to continue for a considerable period of time, severe illness, especially digestive disturbances result. (See above, functional importance of the bile.) Thus with a complete bile fistula, there is the interference with fat absorption. Pawlow (148) observed at autopsies of a number of animals with complete biliary, or intestinal fistulæ, a marked softening and pliability of the bones, which had lead to fractures, especially of the ribs. Looser (149) afterwards examined the bones histologically, and proved that the changes were actually osteoporosis. Schmorl (described by Seidel (150)) observed the same condition with gall bladder fistulæ in man. The osteoporosis in Schmorl's case was differentiated from simple senile bone atrophy by the predominance of the absorptive processes. Thus far, however, it is not known whether this condition is present constantly with gall bladder fistulæ, whether it is due to the absence of some important substance, or to some entirely different cause.

Since cholecystectomy is an operation which removes an organ at one stroke, it is necessary to inquire into the function of this organ in the body economy. Some physiologists think that it serves only to produce mucus (Schröder von der Kolk); others say it regulates the flow of bile (Luciani); still others maintain that the viscid gall bladder bile mixes with the fluid liver bile and slows the current (151). While these writers lay more stress on the mechanical factors of bile flow, others see in the gall bladder a chemical-physiological function because of the increased usefulness of the thickened bile (152). Indeed, according to Hammarsten (153) the content of solids in gall bladder bile is eight times greater than that of liver bile. It is thus clear from the beginning that bile from the gall bladder must contain substances for digestion in greater concentration than liver bile. The experimental removal of the organ has given only



very general results, the workers being content to show that its removal was tolerated, which of course coincides with the fact that in man, small, shriveled, non-functioning gall bladders are frequently found and no clinically demonstrable conditions traceable to its loss can be established (154). Although Rosenberg (155) and Rost (154) could not find any change in the total metabolism of fat and protein after experimental cholecystectomy, Rost, corroborated in the essentials by Klee and Kluppel (156), found that there is an alteration of bile flow, in that bile is constantly being discharged by drops into the intestine. But in some of the cholecystectomized animals a partial "continence" appears after a few weeks; bile is not discharged constantly, but it flows periodically, just as before operation, and the bile stored in the bile ducts enters the duodenum in jets. The interval between two periods of bile flow is short, especially in the first few months, but these pauses gradually lengthen, and finally a rhythmicity may be established which is almost as perfect as in the normal dog with gall bladder intact. This all depends on the functional capacity of the sphincter muscle, first described by Oddi (82), which closes the papilla. If it is strong and functions well, the bile is dammed back and collects in the large ducts, they then enlarge and form a substitute reservoir. But when the sphincter is poorly developed, there is no dilatation of ducts but a more or less constant flow of bile, *i.e.*, there is a much poorer functional result. Rost could show on autopsy material that these same conditions result in man; he also observed that with a poorly functioning sphincter, the danger of an ascending infection increases, and no dilatation of the ducts takes place. We do not know why some of the previously normal animals become continent, while others do not. It should also be mentioned that not only do the bile ducts distend, but the gall bladder stump has a tendency to dilate into a new reservoir, especially when a portion of the cystic duct is left remaining (157).

If continence is established in cholecystectomized animals, the flow of bile is as prompt as in normal animals, but of course the quantity expelled is considerably less, and what is probably more important, all the bile is discharged from the ducts at the first stimulus from the passage of the chyme in the duodenum, and none is left for the remainder of the food except as it is freshly secreted by the liver. Moreover, the bile in the ducts is only slightly concentrated and therefore must be poorer in active solids. Furthermore, Rost has shown that cholecystectomy influences pancreatic secretion, and only about one-third of the normal amount of bile plus pancreatic secretion is discharged, to mix with a certain amount of food. This may possibly be due to exhaustion of the secretin, although why and in what manner secretion is influenced by the removal of the gall bladder, is unknown. This inadequacy of pancreatic and bile



secretion in its turn leads to a stasis of food in the duodenum, which reflexly diminishes the hydrochloric acid production in the stomach (158). This is probably the best explanation for the resulting hydrochloric acid deficiency which now causes numerous general disturbances such as vomiting, eructations, gastric pressure sensations, constipation, etc. (152). These symptoms are frequently attributed to adhesions, although in later laparotomies none can be found; but similar symptoms have been observed, when an aseptic calculus occluded the gall bladder (159).

[The rate at which the gall bladder can concentrate bile has been determined in the ingenious experiments of Rous and McMaster. They found that a gall bladder emptied at the beginning of an experiment and left to fill from the liver concentrated 49.8 c.c. to 4.6 c.c. in about 22 hours. The gall bladder has, of course, often been considered a mere diverticulum in the duct system but it is apparent that its functions are more than that. It, of course, contains smooth muscle within its walls and it is assumed that it squirts its contents into the duodenum when the sphincter of Oddi relaxes. The contrary innervation, as Meltzer termed it, is said to be such that the relaxation of sphincter and contraction of gall bladder take place synchronously. But the experiments of Doyon and others following, have not demonstrated the existence of this mechanism. Indeed, attempts to record contractions of the intact gall bladder are beset with many difficulties and none have succeeded. The movements of respiration give records on tracings which obliterate any which the gall bladder may have made. By removing the organ and suspending it between levers in a bath of oxygenated Locke's solution as done with intestinal segments, etc. a slow contraction and relaxation indicative of ordinary smooth muscle tonus is obtained, but no active contractions. When the papilla of Vater is observed through a duodenostomy with the incision in the abdominal wall closed as far as possible to restore intraabdominal pressure, it will be found that the bile runs out in a tiny stream as the sphincter relaxes and any spurts are absolutely synchronous with inspiration, *i.e.*, when the diaphragm descends it presses the liver downward and squeezes out bile. In general it may be concluded that an expulsive power has never been demonstrated in the gall bladder any greater than the secretory pressure of the liver (250 mm. water). When the sphincter is closed, bile accumulates, and the pressure slowly rises; when the sphincter opens, the bile runs out because of the pressure under which it was confined, plus the pressure against the liver and gall bladder from surrounding structures. Ether was necessarily used in these experiments which were performed on dogs (160).]

The results of *cholecystenterostomy*, by which operation the bile is led into the stomach, small intestine or colon, have been studied experiment-

ally by Viedemann (161), who paid particular attention to digestion as studied through fistulæ. He found that allowing the bile to flow into the stomach did not influence gastric acidity, at least not on a milk diet (see also p. 58). Gastric motility is unchanged immediately after the operation but later shows perceptible slowing. Intestinal digestion is not impaired by bile drainage into the stomach, but appears to be altered when the bile is drained into the small intestine.

In animals, a *cholecystocolostomy* exposes the bile passages to great danger of infection, but in spontaneous ruptures of the gall bladder into the colon, a subsequent cholangitis is not the rule.

Experimental investigations of *hepato-cholangio-enterostomy*, i.e., anastomoses between branches of the hepatic duct and the gastro intestinal canal, were made by Enderlen and Zumstein (162). In normal animals the anatomical structure is not especially favorable for this operation, since the larger ducts are deeply situated under the surface of the liver. But in chronic obstruction the branches are reached more easily.

Intestinal contents have no injurious effect on living liver tissue, which offers an interesting additional fact to the problem of autodigestion of living tissue, discussed above.

When *obstruction of the bile ducts* by calculi or tumors is complete and of long duration, the bile stored in the ducts is often not greenish yellow, but is white. This applies particularly to occlusion of the cystic duct, in which case the gall bladder becomes distended with this clear white fluid (hydrops). But the rare cases of hydrops of the whole duct system from chronic occlusion of the common duct are of greater interest, and more important for the understanding of hydrops formation. Kausch (163) among others has described such a case in detail. It can be deduced that the quantity of bile depends on the secretion of the liver, on the secretion of the bile channels, and on the absorption of bile in the system. The amount of secretion from the bile passages can be very large, as Kausch shows in his case.

There are two opposing theories in reference to the etiology of *white bile* (164). The one asserts that in stasis, the liver cells partially or completely lose the power to form pigments (165). This only applies to occlusion of the common duct. But with this theory it seems inexplicable, as Kausch points out, that the patients are jaundiced and constantly excrete large quantities of bile pigments in the urine. The other theory states that the increase of pressure in the bile passages forces the bile secreted by the liver into the blood and lymph vessels (163), (166), and at the same time the mucosa of the bile passages hypersecretes (167). Hydrops of the gall bladder when calculi occlude the cystic duct, can be explained similarly.

[It seems that the gall bladder and ducts exert opposing influences on the bile; the gall bladder concentrates it, while the ducts dilute it with a thin colorless fluid which they can secrete against considerable pressure. In obstructed ducts either unconnected with the gall bladder or connected to one that is functionless, this fluid gradually replaces the bile and becomes the "white bile" of surgeons (168).]

The subject of *pain in attacks of cholelithiasis* especially that radiating to the shoulder, will be discussed when dealing with the sensitivity of the abdominal cavity.

In 1911, Clairmont and Haberer described a "*bile peritonitis*" (169), although the pathological anatomist could discover no perforation in the bile passages. These authors emphasized, in a later work (170), that there must have been a pathological condition of the walls of the gall bladder and bile channels to permit this abnormal permeability, but its nature was not explained. There was no microscopical investigation of this case, but the authors found a similar bile exudate in the abdomen in four dogs whose common bile ducts had been ligated for other reasons. Since attention was called to this condition, reports of similar cases were rapidly forthcoming, and two years later, Sick and Frankel (171) were able to collect 18 cases in the literature and the number has since increased. The common feature in all is the biliary peritonitis, but opinions differ as to the etiology. Clairmont and Haberer in their second publication, group the pathological anatomical findings into those in which either an opening was found macroscopically in the bile passages or in which leakage was proved microscopically, sometimes, however, only in the form of a subserous bile passage on the liver surface. But there still remained cases in which neither perforation nor inflammation could be found, and in which it was apparently a question of diffuse permeability (for instance, the case of Schievelbein-Ritter (172)). Since the perforations found were often exceedingly minute, and only visible microscopically, the majority of authors are inclined to assume that a perforation is a constant feature and may have been overlooked in the cases in which it was not found (173). A new light is shed on the question by Blad's (174) investigations. He showed first in vitro, that the pigments in the colloidal bile cannot pass through a membrane. But when tryptic enzyme (Pancreon) is added and the colloids are destroyed, the pigment is "liberated" in some obscure way, and passes through the membrane. Furthermore, when a freshly removed gall bladder was used as a diffusion sac, the colloid would not pass through, while the crystalloids did very easily. He then elaborated these results in vivo by ligating the choledochus and injecting a tryptic enzyme into the gall bladder of dogs by way of the liver (duodenal juice plus bacteria). In another experi-

mental series, he injected the same ferment into the gall bladder through the papilla of Vater. An actual biliary peritonitis without perforation of the bile passages resulted. The gall bladder wall showed no inflammation but was completely necrotic. Further observations must show whether this explanation holds good for all human cases. That reported by Risel (175) in which there was a sterile circumscribed gangrene of the gall bladder might be utilized in this connection, although the author himself believes it might have been a thrombotic process in the cystic artery. At any rate, necrosis of the gall bladder wall alone does not lead to an escape of bile, as is shown by a case of volvulus of the gall bladder, in which, in spite of total necrosis of the mucosa, submucosa and muscularis, no bile was found in the abdominal cavity (176). Many cases of suppurative cholecystitis illustrate the same point.

The oldest discussion of the reaction of the peritoneum to bile is probably that of Bohn who attempted to discover why gall bladder injuries are usually fatal (177). He concluded from investigations on dogs, the gall bladders of which he removed with and without ligation of the cystic duct, that gall bladder injuries prove fatal, because bile escapes into the abdominal cavity (for other early experiments, see Rost, 81). Recent investigations are discussed by Erhard and Notzel (178). Furthermore, all cases of gall bladder perforations in man, and there are many in the literature, can be used in this study. Ehrhard and Notzel found that normal sterile bile does not call forth an inflammatory reaction in the peritoneum but the moment infectious organisms enter with the bile, a severe peritonitis begins. In fact Notzel showed that animals intraperitoneally inoculated with bacteria of a certain virulence, remained living, but those treated similarly, but with addition of bile, all succumbed. These experimental findings correspond with clinical observations, and Hirschel (179) for example, reported eight cases of peritonitis originating from the gall bladder, all of them ending fatally. On the other hand, the prognosis is by no means so unfavorable in traumatic perforation of the gall bladder or in a ruptured hydrops. Such traumatic lesions, especially experimental ones, heal very promptly, a fact which was already observed by older authors. Enderlen and Justi (180) have studied the histology of healing in gall bladder wounds.

In injuries to the liver, the escape of bile is of much less importance than hemorrhage. For this reason, the slowing of the pulse, reported by Finsterer (181) on the basis of clinical and experimental observations is not always found (see investigations by Rubaschow (182)).



## LITERATURE TO LIVER AND GALL BLADDER

1. Compilation and Lit. see Fischler: Physiologie u. Pathologie der Leber, Springer's Verlag., 1916.
2. Hess: v. Volkman's Sammlung klin. Vorträge, N. F., 1900, No. 576.
3. Kehr: Handbuch d. prakt. Chirurgie, 3, p. 611, 4 Edit.
4. Gluck: Arch. f. Klin. Chir., 1883, 29, p. 129.
5. Ponfick: Virchows Archiv., 1889, V. 118 and 119.
6. Thoele: Neue deutsche Chirurgie, 1912, V. 4, p. 70.
7. Claude Bernard: Compt. rend. de l'Acad. des Sciences, 1848, V. 27, p. 514 and L'oeuvre de Claude Bernard (Paris Bailliere et Fils).
8. see Pflüger: Das Glykogen und seine Beziehungen zur Zuckerkrankheit, 1905 2 Edit. and Abderhalden, Physiologische Chemie, 2, p. 409, espec. p. 430.
9. Isaac, S.: "Die Funktionsprüfung der Leber," Berliner klin. Wochenschrift, 1913, p. 1167.
9. Sachs: Ztschrft. f. klin. Med., V. 38, p. 87.
9. Hohlweg: Deutsches Arch. f. klin. Med., 1907, 3, p. 183.
10. see Wohlgemuth in Oppenheimers Handbuch d. Biochemie, 3, p. 178.
11. E. Abderhalden und London: "Weitere Versuche zur Frage nach der Verwertung von tief abgebautem Eiweiss im tierischen Organismus, ausgeführt an einem Hunde mit einer Eck'schen Fistel," Zeitschr. f. physiol. Chemie, 1907, 54, p. 112.
12. see van Slyke, D. D.: "Chemistry of the proteins and their relation to disease," Oxford Medicine, V. 1, p. 251.
13. v. Schroder: Arch. f. exp. Path. u. Pharmak., 1882, 15, p. 364.
14. see Abderhalden: Physiol. Chemie, 1909, p. 316 und Wohlgemuth in Oppenheimers Handbuch der Biochemie, 1907, 3, p. 183.
15. Nencki und Pawlow: Archiv. f. exp. Path. u. Pharmak., 1893, V. 32. 16.
16. J. Frankel: Chemie der Lebensvorgänge Dynamische Biochemie; Wiesbaden, 1911, p. 383, J. F. Bergmann.
16. K. Glassner und Singer: Med. Klinik., 1909, No. 51.
16. M. Landau und Mc Nee, J. W.: "Zur Physiologie des cholesterin Stoffwechsels," Ziegler's Beitr. zur prakt. Anat., 1914, V. 58, 667-699.
16. Aschoff-Bacmeister: Die Cholelithiasis, Jena, 1909.
17. Schiff: Arch. des sciences physique et naturelle, 1877, 58, p. 293.
18. Lebedeff: Arch. fur (Anat. u.) Physiol., 1883, V. 31, p. 11.
19. Fischler, F.: "Ueber das Wesen der zentralen Lappchennekrose in der Leber und über die Rolle des Chloroforms bei dem sogenannten Narkosenspattod," Mitt. a.d. Grenzgebieten, 1913, 26, p. 553 (further lit.).
20. G. H. Whipple and Sperry, J. A.: "Chloroform poisoning; liver necrosis and repair," John Hopkins Hosp. Bull., 1909, 20, p. 278-289.
21. Adamski, Johann: "Lebernekrosen bei Pankreas fettgewebsnekrose," Dissert. Munchen, 1912, C. Wolf and Sohn.
22. Guleke: Arch. f. kl. Chir., V. 83, p. 602.
23. Lusk Graham: "The Elements of the Science of Nutrition," 1917, Ed. 3.
23. Davis, N. C., Hall, C. C., Whipple, G. H.: "The rapid construction of liver cell protein on strict carbohydrate diets, etc." Archiv. Int. Med., 1919, 23, 689 and 711; 1921, 27, 679; 1921, 28, 21.
24. Doyon: Oppenheimers Handbuch d. Biochemie, 1908, 2, 2.
25. Morawitz: Ergeb. d. Inn. Med., 1913, 10.
25. Nolf, P.: "Eine neue Theorie der Blutgerinnung," Ergebnisse der inneren Med., 1913, 10; Ergebnisse der inneren Med., 1912, 9, 275-341.

25. Doyon: "Rapports du foie avec la coagulation du sang," Journ. de Physiol. Pathol. gen., 1912, 14, p. 229.
26. for Lit: s. Kehr, neue deutsche Chir., 8, p. 150.
27. Rio Branco: Essai sur l'anatomie et la médecine opératoire du tronc cœliaque et ses branches, etc., Paris, Steinheil.
28. Ehrhardt: Arch. f. klin. Chir., 1902, V. 62, p. 460. Janson: Zieglers Beiträge, 1895, V. 17, p. 505. Haberer: Arch. f. klin. Chir., V. 78, p. 557. Narath: Brun's Beiträge, V. 65. Narath, II: Deutsche Zeitschft. f. Chir., 1916, V. 135. Cohenheim and Litten: Virchows Arch., 1876, 67, 153.
29. Nicollelli: Centralbl. f. d. Grenzgebiet, 1910, 13.
30. Thole: Chirurgie d. Lebergeschwulst Neue deutsche Chirurgie, V. 7.
31. Kehr: cit. see Kehr. Chirurgie d. Gallenwege, neue deutsche Chir., 8, p. 155; Munch. med. Wochenschrift., 1903.
32. Bourdenko: cited by Kehr, 31.
33. Narath II und S. Steckelmacher: "Experimentelle Nekrose und Degeneration der Leber. Versuche mit vitaler Toluinblaufärbung," Zieglers Beiträge, 1913, V. 57, 314-344.
34. cf. Lissauer: Deutsche Zeitschrift. f. Chir., 1916, V. 35.
35. Tappeiner: Arbeiten aus d. physiol. Anstalt. Leipzig, 1873, V. 7.
36. Claude Bernard: Comptes rendus, 1850.
36. De Josselin de Jong: "Ueber die Folgen der Thrombose im Gebiete des Pfortadersystem," Mitt. a.d. Grenzgebieten, 1912, V. 24 (Steenhuis, Dissert Groningen, 1911).
36. Erhard: Arch. f. klin. Chir., 1902, 68, p. 462.
37. Solowieff: Virchows Arch., 1875, V. 62.
38. Lit. Fischler: Lebercirrhose in Ergebn. d. inn. Med., 1909, V. 3 und Lissauer, Berlin. kl. Wochenschrift., 1914 (collected ref.).
39. Cohnheim und Litten: Cohnheim, ges. Abhandlungen.
40. Zahn: Naturforscherversammlung, 1897, p. 9.
41. Chiari: Zeitschft. f. Heilkunde, 1898, V. 19, p. 475.
42. Josselin de Jong and Sax, R.: Zentralbl. f. Path., 13.
42. Enderlen, Hotz, und Magnus-Alsleben: "Die Pathologie und Therapie des Pfortaderverschlusses. Experimentelle Untersuchungen über die Ecksche Fistel," Ztschft. f. d. ges. exp. Medizin, 1914, V. 3.
43. Verse: Zieglers Beiträge, V. 48.
44. Langenbuch: Deutsche Chirurgie, 45, V. 2, p. 106.
45. E. Magnus-Alsleben: Ueber die Ecksche Fistel, Verhandlung d. deutsch. Kong. f. innere Med., 1912, 29, 572-579; Lits. Fischler, Arch. f. exp. Path. and Pharmak 61; Arch. f. klin. Med. 104 and 111; Franke u. Rabe, Sitzungsberichte u. Abh. d. Naturforschenden Gesellsch. zu Rostock, 1912, Enderlen, Hotz u. Magnus Alsleben, Zeitschr. f. d. ges. Exp. Medizin, 1914, 3.
46. Rosenstein: Arch. f. klin. Chir., 98.
47. Heller: Arch. f. klin. Med., 1870, V. 7.
47. Ribbert: Zentralbl. f. allg. Pathol., 1897.
47. Arnold: Virchows Arch., V. 124, p. 385.
48. Cases of Schuppel, Hainski, Lange, Thran, Umbreit, Eisenmenger: Lit. see Fischler (1), p. 256.
49. Cosentino: Cited by Thole, Leberverletzungen Neue deutsche Chir., 4, p. 101. Borgzecky: Brun's Beiträge, V. 88, p. 466. Baron: Zentralbl. f. Chir., 1910.
50. Ransohoff, J.: Ann. of. surg., 1908, 98, 247-257, 4 pl.

51. Hopfner, E.: Der Aszites u. seine chirurgische Behandlung, *Ergebn. d. Chir.*, 1913, 6, 410-480.
52. Quincke: *Therapeut. Monatshefte*, July, 1914.
53. see Klopstock. *Berliner kl. Wochenschrft.*, 1911, No. 3.
54. Lubarsch: *Naturforscherversammlung*, 1912 Munster.
55. Ito und Omi: *Deutsche Zeitschrft f. Chirurgie*, V. 62.
56. Josselin de Jong: *Mitt. a.d. Grenzgebieten*, V. 24.
57. Talma: *Berliner klin. Wochenschr.*, 1900, 1898. Drumond: *Brit. med. Journal*, 1896.
58. Tillmann: *Deutsche med. Wochenschr.*, 1899.
59. Schiff: *Neuere Schweizerische Ztschrft. f. Heilkunde*, 1862, V. 1. Ore: *Compt. rend. de l'Academie*, 1856, V. 42. Golowieff: *Virchows Arch.*, 1875, V. 62.
60. Rosenstein, P.: "Ueber die Behandlung der Lebercirrhose durch Anlegung einer Eck'schen Fistel," *Arch. f. klin. Chir.* Berlin, 1912, 98, 1082-1092. *Chirurgenkongress*, 1912.
61. Bunge: "Die Talma—Drummondsche Operation; Ihre Judikation, Technik, und die bisher erzielten Resultate," *Wiener klin. Wochenschr.*, 1905, 18, 930. *Klinisches Jahrbuch*, 1905, 14.
62. Ewald: *Ueber Fruzeitige Punction von Aszites*, Berlin. *klin. Wochenschrift*, 1888, 16.
63. Rouotte: *Lyon med.*, 1907, 109, p. 40.
64. Franke: *Chirurgenkongress*, 1911. Handley, W. S.: "Abstract of the Hunterian lectures on the surgery of the lymphatic system," *Lancet*, April, 1910.
65. "Die funktionelle Bedeutung der Gallenblase. Experimentelle und anatomische Untersuchungen nach Cholecystectomie," Rost, *Mitt. a.d. Grenzgeb.*, 1913, v. 26, Lit. Babkin: *Aeusserer Sekretion der Verdauungsdrusen*, Springers Verlag, 1914.
66. Hammarsten, O.: "Zur Chemie der Galle," *Ergebnisse d. Physiologie*, 1905, V. 4, p. 14.
67. Wohlgemuth: *Oppenheimers Handbuch d. Biochem*, 1908, 3, 1 p. 202, Jena, 1909, G. Fischer.
68. Naunyn: *Klinik. der Cholelithiasis*, 1892.
69. Aschoff: "We entstehen die reinen Cholesterinsteine?" *Munchener med. Wochenschr.*, 1913 (with compilation).
70. Rabe: *Festschrift. z. Feier des 25 jahr. Bestehung d. Eppendorfer Krankenhauses*, 1914.
71. Barbera: *Arch. ital. de Biol.*, V. 26 and 31 und *Bull. delle Sc. med. di Bologna Serie T.* 7, 1896, 1898.
72. Weintraud: In v. Noordens *Handbuch d. Pathol. u. Stoffwechsels*. Thorspecken: *Mitt. a.d. Grenzgebieten*, 1909, V. 19. Letienne und Hanot: *Arch. generales de med.*, 1885, V. 1.
73. Ostwald Adolph: *Lehrbuch der chemischen Pathologie* Veit and Co., Leipzig, 1907.
74. Majo Robson: *Zentralbl. f. Physiol.*, 1890, V. 4, p. 634.
75. Brand: *Pflugers Arch.*, 1902, 90, p. 494.
76. see Stadelmann, *Der Ikterus*, p. 81; Babera, *Bull. della Sc. med. di Bologna*, 1898.
77. Rosenberg: *Arch. f. Physiol.*, 1901, p. 528.
78. Minkowski: *Deutsche Klinik.*, V. 5, p. 681. Pfaff u. Balde: *J. of exp. Med.*, V. 2, p. 49. Schiff: *Pflugers arch.*, 1870, V. 3, p. 598. Tappeiner: *Arbeiten a. d. physiol. Institut. Leipzig*, V. 7. Stadelmann: *Deutsche med. Wochenschrft.*, 1896, *Zeitschrft. f. Biol.*, 1897, 34, p. 1, *Berliner Klin. Wochenschrft.*, 1896, p. 9-10. Doyon und Dufort: *Arch. de Physiol.*, V. 9, p. 562.

79. Barbera: Zeitscht. f. Biol., 1897, V. 32. Bohm, P.: "Ueber die feineren Bau der Leberzellen bei verschiedenen Zuständen; zugleich ein Beitrag zur Physiologie der Leber, Zeitscht. f. Biol., 1908, V. 51, 409-434. Asher: Zeitscht. f. Biol., 1903, V. 45; Zentralbl. f. d. ges. Physiol. u. Pathol. d. Stoffwechsels, 1911, No. 5. Pletnew: Bioph. Zeitscht., 1909, 21. Loeb, A.: "Ueber den Eiweissstoffwechsel des Hundes und über die Abscheidung der Galle bei Fütterung mit Eiweiss und Eiweissabbauprodukten mit besonderer Berücksichtigung der zeitlichen Verhältnisse," Ztschrft. f. Biol., 1910, V. 55. Kusmine: Ztscht. f. Biol., V. 46.
80. Rost, F.: "Die funktionelle Bedeutung der Gallenblase. Experimentelle und anatomische Untersuchungen nach Cholecystectomy," Mitt. aus d. Grenzgeb., 1913, 26, p. 736. Henri und Portier: Compt. rend. Soc. de Biol., 1902, 54, p. 620.
81. Rost: Die funktionelle Bedeutung d. Gallenblase. Mitt. a. d. Grenzgebieten, 1913, 26, 5. Pawlow: Die Tätigkeit der Verdauungsdrüsen, Wiesbaden, 1892. Cohnheim und Klee: Heidelberger Akad. d. Wissenschaften. Math. naturm. Klasse, 1912.
82. Oddi: Arch. ital. de Biol., 1887, p. 317; also Helly, Arch. f. micr. Anat. V. 54, p. 614 und Hendriksen, Anat. Anz., 1900, V. 17, p. 197.
83. P. Klee und O. Klupfel: "Experimenteller Beitrag zur Funktion der Gallenblase," Mitt. aus d. Grenzgebieten, 1914, 27, p. 783.
84. Doyon: Arch. de Phys., 1896, V. 5, p. 678 and V. 6, p. 19.
85. Bainbridge and Dale: Journ. of Physiol., 1908, V. 33, p. 138.
86. Courtade and Guyon: Compt. rend. Soc. de Biol., V. 60, p. 399.
87. Dogiel: Arch. f. Anatomie, 1899, p. 130. Dogiel: Compt. rend. Soc. de Biol., 1903, V. 55, p. 314.
88. F. Reach: "Untersuchungen zur Physiologie und Pharmakologie der Gallenwege," Zentralbl. f. Physiol., 1912, V. 26. Wiener Klin. Wochenschrft., 1914. Dastre: Arch. f. Physiol., 1889, V. 22, p. 800.
89. Mayo Robson: Zentralbl. f. Phys., 1890, V. 4, p. 634. Copemann and Winston: Journ. of Physiol., 1889, V. 10, p. 213.
90. Munk: Ueber die Resorption von Fetten und festen Fettsäuren nach Ausschluss d. Galle v. Darmkanal. Virchows Arch., V. 122, p. 302. (Lit.)
91. Claude Bernard: cited by Hammarsten, Physiol. Chemie, 1895, 3, Ed., p. 275.
92. Dastre: Du rôle de la bile dans la digestion de matières grasses, Compt. rend. Soc. de Biol., 1887, December.
93. Lewin: Ueber den Einfluss d. Galle und des Pankreassaftes auf die Fettresorption im Dünndarm, Pflügers Arch., V. 63, p. 171.
94. Magnus: Die Wirkung synthetischer Gallensäure auf die pankreatische Fettspaltung, Zeitschr. f. phys. Chemie, V. 48, p. 376.
95. Hammarsten: Ueber den Einfluss der Galle auf die Magenverdauung, Pflügers Arch., 1870, V. 3, p. 53.
96. Rashford and Southgate: Med. Rec., Dec., 1895.
96. Delezenne: Compt. rend. de la Soc. de Biol., 1902, 54, p. 392. Bruns: Arch. de Science biol., 1899, 8, p. 97.
97. Roger, H.: Gaz. d. hopitaux, 1910, p. 1516. Sidney, Martin, and Dawson, William: Proc. of the Roy. Soc., 5, 1, 45, p. 292, V. 48, p. 358.
98. Nepper: Ztscht. f. Biol., 1908, V. 51, p. 1. K. Glassner and G. Singer: "Gallen-säuren als Abfuhrmittel," Wiener klin. Wochenschrft., 1910, 23, 5. Schupbach: Presse med., 1913, V. 21, p. 137-139.



99. Abderhalden: *Physiol. Chemie*, Edit., 1904, 2, p. 690.
100. Lit. see Stadelmann: *Der Ikterus*, Stuttgart, 1891, also Kretz in *Handbuch d. allgem. Path.* 22, 466; Quincke in *Nothnagels Handbuch*, 1899, 18.
101. Eppinger: *Zieglers Beitrage*, V. 31, p. 230.
102. Fleischl: *Bericht über d. Verh. d. kgl. sachs Ges. d. Wiss. zu Leipzig*, 26
103. Hurley: *Arch. f. Anatomie u. Physiol.*, 1893, p. 291.
104. Courvoisiers sign Kasuistisch—statistische Beitr. *S. Pathol. u. Therapie d. Gallenwege*, Leipzig, 1890.
105. McMaster, P. D. and Rous, P.: "Biliary obstruction required to produce jaundice," *J. Exp. Med.*, 1921, 33, 731.
106. Minkowski and Naunyn: *Arch. f. exp. Pathol. u. Pharmacol*, 1886, 21.
107. McNee, I. W.: "Giebt es einen echten hematogenen Ikterus?" *Mediz. Klinik*, 1913, p. 1125-1129. Lantz: *Zentralbl. f. Chir.*, 1907, p. 617.
108. Eppinger: *Zieglers Beitrage*, V. 33. von den Berg, A. A. H., Snapper, I.: "Untersuchungen über den Ikterus," *Berlin. klin. Wochenschrift*, 1914, V. 24, p. 25 and Vol. 51, 1109-1180.
109. Kretz: *Ergebn. d. allg. Pathol.*, No. 8.
110. Stadelmann: *Verhandt. d. med. Kongress*, 1892, 11. Pick: *Wiener klin. Wochenschrift.*, 1874, 29, No. 26. Minkowski: *Verhandt. d. med. Kongress*, 1892, 11. Liebermeister: *Deutsche med. Wochenschrift.*, 1893, No. 16.
111. Tischner: "Vergleichende Untersuchungen zur Pathologie der Leber," *Virchows Archiv.*, 1904, V. 175, 90-184. Tsunoda, I.: "Eine experimentelle Studie über die Folgen der Stenose oder Obliteration des Ductus choledochus; zur Kenntniss der sog. biliaren cirrhose," *Virchows Archiv.*, 1908. Nasse: *Arch. f. klin. Chir.*, V. 48, p. 886. Siegerbeek von Heukelom: *Zieglers Beitrage z. pathol. Anatomie*, 1896. Frerichs: *Klinik. d. Leberkrankheiten*. Beloussow: *Arch. f. exper. Pathol. u. Pharmacol.*, 1881, V. 14. Bauer: *Inaug. Diss. Rosstock*, 1882.
112. Frey und Harley: *Verh. d. 11. med. Kongr.*, 1892, p. 115 and *Arch. f. (Anat. u.) Physiol.*, 1893, p. 291.
113. Burger and Fischer: *Ztschft. f. d. ges. exper. Med.*, 1914, V. 3.
114. Rywosch: *Arbeiten d. Pharmacol. Instit. in Dorpat*; Lit. in Stadelmann: *Der Ikterus*, p. 264.
115. See Krehl: *Pathol. Physiol.*, 1912, p. 372, F. C. W. Vogel.
116. P. Morawitz and Bierich: "Ueber die Pathogenese des cholacemischen Blutungen," *Arch. f. exp. Path.*, 1907, V. 56, p. 115.
117. Kunika: *Deutsche Zeitschft. f. Chir.*, 118.
118. Clairmont and Haberer: *Mitt. a. d. Grenzgebieten*, 1911, V. 22, p. 159.
119. Meckel v. Helmsbach: *Mikrogeologie* herausgegeben von Billroth, 1856.
120. H. Schade: "Ueber Konkrementbildungen beim Vorgang der tropfigen Entmischung von Emulsionskolloiden," *Munchener med. Wochenschrift*, 1909, No. 1 and 2 and 1911, No. 14; *Ztschft. f. exp. Pathol. u. Therapie*, 1910, 8, u. *Kolloid-chemische Beihefte*, 1, p. 375.
121. L. Aschoff-Bacmeister, A.: "Die Entstehung des Gallenstein-Leidens," *Die Cholelithiasis*, Jena, 1909; Bacmeister: *Ergebn. d. inn Med.*, 1913, 11, p. 1, 1-31, 1 pl.; Lit. see Riese: *Ergebn. d. Chir.*, 1913, 3.
122. Aschoff, L.: "Zur Frage der Cholesterinbildung in der Gallenblase," *Munchener med. Wochenschrift.*, 1906, 13, 1847; also *Mitt. aus d. Grenzgebieten*, 1912, 24.
123. L. Hofbauer: "Zur Pathogenese der Cholelithiasis," *Mitt. a. d. Grenzgebieten*, 1912, v. 24.

124. Lichtwitz, L.: "Experimentelle Untersuchungen über die Bildung von Niederschlägen in der Galle," *Deutsches Arch. f. klin. Med.*, 1907, V. 92, 100-108; *Deutsche med. Wochenschr.*, 1910, p. 704.
125. A. Exner u. Heyrowsky, H.: "Zur Pathogenese der Cholelithiasis," *Arch. f. klin. Chir. Berl.*, 1908, 86, 609-642; *Chirurgenkongress*, 1908, and *Berliner klin. Wochenschr.*, 1908.
126. Larroche: cited by Bacmeister, *Ergebn. d. inn. Med.*, 11, p. 14. Chauffard: *Inners. Kongressblatt*, 9, p. 44.
127. Naumann: *Wiener kl. Wochenschr.*, 1912. McNee, T. W.: "Zur Frage des Cholestearingehalts der Galle während der Schwangerschaft. Mitt. Bemerkung von L. Aschoff," *Deutsche Med. Wochenschrift*, 1913, 39, 994-996.
128. Chalatoff: *Chir. Kongressblatt.*, 1914, 4, p. 561.
129. Verse: *Munchener Med. Wochenschrift*, 1916.
130. Kretz: *Handbuch d. allgem. Pathologie*, 2, p. 493.
131. Boysen, I.: "The pathogenesis of gallstones (Swedish)," *Inneres Kongress zentralblatt*, 1914, 11, p. 121.
132. Aschoff, L.: "Wie entstehen die reinen Cholesterinsteine?" *Munchener med. Wochenschr.*, 1912, p. 1753 u. 1913, No. 32.
133. Kuru: *Virchows Arch.*, 1912, V. 210, p. 433.
134. Ooyama, T.: "Zur Frage der Cholelithiasis," *Zieglers Beitrage*, 1913, V. 57.
135. Aufrecht: *Deutsches Arch. f. klin. Med.*, 1919, V. 128.
136. v. Hanseemann: *Virchows Arch.*, V. 212, p. 319.
137. Glaessner: *Wiener klin. Wochenschrift*, 1918, p. 549.
138. Conradi, H.: "Ueber Zuchtung von Typhus bacillen aus dem Blut mittels der Gallenkultur," *Zentralbl. f. Bact.*, 1906.
139. Frankel-Krause: *Zeitschrift. f. Hygiene*, 1899, V. 32, p. 106.
140. Laubenheimer: *Zeitschrift. f. Hygiene*, V. 58, p. 64.
141. Forster, I.: "Ueber die Beziehungen des Typhus und Paratyphus zu den Gallenwegen," *Munchener med. Wochenschrift.*, 1908, No. 1-6.
142. Hendel: *Arbeit. aus. d. Kais. Ges. Amt.*, 1908, V. 28.
143. Ehret and Stolz: *Mitt. a. d. Grenzgeb.*, V. 6, 7, 8, 10.
144. Koch: *Ztschft. f. Hygiene*, V. 60.
145. Gobel, C.: "Ueber Leberabscesse," *Mitt. a. d. Grenzgebieten*, 1906, V. 15, 521-563.
146. Wilms: "Venenunterbindung bei eitriger Pfortaderthrombose nach Appendicitis," *Zentralbl. f. Chir.*, 1909, p. 1041-1043.
147. Clara Reiniger: "Ueber die Entstehung von Leberabscessen auf rücktaugigen Wege," *Frankfurter Zeitschrift f. Pathol.*, 1913, V. 13, 103-113.
148. Pawlow: *Verhandt. d. Med. Gesellschft. in St. Petersburg*, 1905.
149. Looser, E.: "Ueber Knochenveränderungen bei chronischen Fisteln der grossen Verdauungsdrüsen," *Verh. d. Deutschen pathol. Ges.*, 1907.
150. H. Seidel: "Permanente Gallenfistel und Osteoporose beim Menschen," *Munchener Med. Wochenschrift.*, 1910, p. 2034.
151. Billard and Cavillie: *Compt. rend. Soc. de Biol.*, 1900, p. 595, and 625 and 780.
152. H. Hohlweg: "Ueber Störungen der Salzsäureabscheidung des Magens bei Erkrankungen und nach Exstirpation der Gallenblase," *Deutsches Arch. f. klin. Med.*, 1912, 108, p. 255.
153. Hammarsten: *Nova acta Reg. Soc. scient. Upsala*, 1894.
154. See *Zur Geschichte d. experimentellen Cholecystectomy*. Rost, *Mitt. aus d. Grenzgebieten*, 1913, 26, p. 712.
155. Rosenberg: *Pflugers Archiv.*, 1893, 53, p. 388.

156. P. Klee and O. Kluppel: "Experimenteller Beitrag zur Funktion der Gallenblase," Mitt. a. d. Grenzgebieten, 1914, 27, p. 785.
157. Nasse: Arch. f. klin. Chir., 1884, 48, p. 885. Oddi: Bull. de sc. med. Bologna, 1888. Florken: Deutsche Zeitschr. f. Chir., 113, p. 604. v. Stubenrauch: Arch. f. klin. Chir., 82, p. 667. De Voogt: Nederl. Tydschr. voor Geneeskunde, 1898, 2, p. 236. Clairmont and Haberer: 33 Chirurgenkongress, 1904.
158. Cohnheim and Marchand: Zeitschrift. f. physiol. Chemie, V. 63, p. 41.
159. Riedel: "Der Gallenstein in Keimfreier Gallenblase," Munchener Med. Wochenschr., 1912, p. 8.
160. Rous, P. McMaster, P. D.: "Concentrating activity of the gall bladder," J. Exp. Med., 1921, 34, 47, see also Auster and Crohn, Proc. Soc. Exp. Biol. and Med., 1921, 19, 117.
161. Wiedemann: "Experimentelle Untersuchungen zur Lehre der Verdauung und Resorption verschiedener Nahrungsprodukte bei abnormalem Gallenzufluss in der Verdauungsapparat," Brun's Beitrage, 1914, V. 89, p. 594.
162. Enderlen and Funstein "Ein Beitrag zur Hepato-Cholangio-Enterstomie und zur Anatomie der Gallengange," Mitt. a. d. Grenzgebieten, 1904-1905, V. 14, 104-119.
163. W. Kausch: "Die Hydrops der Gesamten Gallensystems bei chronischem Chole-  
dochusverschluss und seine Bedeutung fur den Chirurgen," Mitt. a. d. Grenz-  
gebieten, 1911, V. 23.
164. Korte, W.: Beitr. z. Chir. d. Gallenwege u. d. Leber, 1908. Courvoisier: Kasuis-  
tische usw. Beitrage. z. Chirurgie d. Gallenwege, 1890.
165. Steiner: Wiener klin. Wochenschr., 1914, No. 23.
166. Quincke: Die Krankheiten der Leber in Nothnagels spec. Path. u. Ther., 18.  
Bertog, J.: "Beitrag zur Frage der Entstehung der sogen. weissen Galle bei  
absolutem dauernden Choleodochusverschluss," Mitt. aus. d. Grenzgebieten,  
1913, V. 26.
167. Berg: "Mitt. aus d. Grenzgebieten, 1912, V. 24.
168. Rous, P. and McMaster, P. D.: "Physiol. causes for varied character of stasis  
bile," J. Exp. Med., 1921, 34, 75.
169. Clairmont u. Haberer: Grenzgebiete, 1911, V. 22, p. 154.
170. Wiener klin. Wochenschrift., 1913, p. 891.
171. P. Sick and Frankel: Bruns Beitrage, z. klin. Chir., 1913, V. 85.
172. Schiebelbein-Ritter: "Ueber galliche Peritonitis ohne Perforation der Gallen-  
wege," Bruns Beitrage, 1910, V. 71.
173. C. Nauwerk and Leibke: "Giebt es eine gallige Peritonitis ohne Perforation der  
Gallenwege?" Berliner klin. Wochenschr., 1913, P. 624-627.
174. Blad: Archiv. f. klin. Chir., 1917, 109, 101.
175. Risel: Deutsche med. Wochenschrift., 1914, p. 1599.
176. G. Kubig: "Ueber Volvulus der Gallenblase," Munchener med. Wochenschrift.,  
1912, 59, 1998-2000.
177. Bohn: De renunciatione valnerum, Leipzig, 1755.
178. W. Notzel: "Experimentelle Untersuchung zur Gallenblasen perforation peri-  
tonitis," Arch. f. klin. Chir., 1910, V. 93. Ehrhard: Arch. f. klin. Chir., V. 64,  
and 74.
179. G. Hirschel: "Die Behandlung der diffusen eitrigen Peritonitis mit 1% Kamp-  
feroel," Bruns Beitrage, u. Munchener med. Wochenschrift., 1910, V. 56.
180. Enderlen u. Justi: Deutsche Zeitschrift. f. Chir., V. 61.
181. Finsterer: Deutsche Zeitschrift., V. 121.
182. S. Rubaschow: "Ueber Bradykardie bei Leberverletzungen (Erwiderung auf die  
Arbeit von H. Finsterer)," Deutsche Zeitschr. f. Chir., 1913, V. 120, p. 515.

## CHAPTER V

### SPLEEN

**Splenectomy** is doubtless the most frequent operation performed on the spleen (1). It was first done for injuries which without operative interference, would usually have proved fatal from hemorrhage. Generally speaking, removal of the spleen is well borne, except in young animals (sucklings) which perhaps show some *retardation of growth*. But in this case the laparotomy itself, and not the extirpation of the spleen, may cause this disturbance (2). As an immediate consequence, vomiting of bloody gastric contents has been reported (3), to be explained perhaps by a retrograde thrombosis into the gastric vessels such as occurs in resections of the omentum (v. Eiselberg, see later). Nevertheless, the loss of so large an organ is not without its results and study of the sequelæ of splenectomy has materially increased our knowledge of its physiology. This better knowledge has led to more operative removals of the organ and has enabled us to cure or improve a number of diseases of the spleen, or rather, a number of general diseases in which the spleen occupies an important place, *e.g.*, pernicious anemia, etc. Thus, splenic surgery has gained steadily in importance during recent years.

Since the spleen has such an extraordinarily rich blood supply, it is natural that attention is directed to changes in the *peripheral blood picture*, but the data collected by various writers is not uniform concerning the effect of splenectomy on either the hemoglobin or the number of red blood corpuscles. This depends possibly, as Asher (4) and Vogel (5) have shown, on a relation between the iron content of the food and blood regeneration, inasmuch as the hemoglobin and the red blood cells remain steadily low on a diet poor in iron. In general, a diminution in the number of erythrocytes and in the percentage of hemoglobin, which is usually ascribed to the loss of blood from operation, is observed immediately after splenectomy (6). According to Vulpus (7), this diminution in erythrocytes is never more than 20 per cent., and in one month it is again restored to practically the pre-operative count; Kuttner (8) actually records a count of 6,650,000 with 130 per cent. hemoglobin a year after splenectomy for gunshot injury; this probably can be related to the removal of its blood destroying activities. Peres (9) also describes a case in which there was a very rapid regeneration of hemoglobin.



But these are in the minority; the results in humans, as confirmed by many experiments on animals, may be summed up by saying that after splenectomy there is only a transient and minor diminution in hemoglobin and in the number of red blood corpuscles, which is completely compensated in a short time (lit. see Vulpus (7), p. 687).

[An increased resistance of the red blood cells to hypotonic salt solutions, hemolytic sera, saponin, etc. has been found after splenectomy. Careful studies of this phenomenon have shown that this property resides in the red blood cell itself and is not due to an antihemolytic power of the serum or other similar factors. Its explanation is not clear but it is probably of importance in the decreased tendency to hemoglobinuria and jaundice seen after the administration of hemolytic agents (10).]

Changes in the number and variety of *white blood cells* are found much more regularly than changes in the erythrocytes (Ehrlich (6)). Soon after operation, there appear a lymphocytosis and an eosinophilia which persist for many months, indeed for years (11), and which disappear very gradually. The absolute number of the leucocytes is also considerably increased. The reason is said to be a stimulus engendered by the removal of the spleen, which acts on the organs particularly concerned in the formation of lymphocytes and eosinophiles, *i.e.*, on the bone marrow and lymph nodes. In monkeys, however, Kreuter (12) observed no influence on the peripheral blood picture; there was only a slight eosinophilia and no lymphocytosis at the end of the observation period. It seems, however, that physiologically, monkeys have a lymphocytosis.

A similar change in the blood picture, *i.e.*, lymphocytosis and eosinophilia, can be produced experimentally by the injection of substances which "act by increasing the tonus of the autonomic nerves," while conversely, a polymorphonuclear leucocytosis and an a-eosinophilia, result from substances which increase the tone of the sympathetics and exert an intensive stimulation on the bone marrow (13). Substances which are able to influence the blood picture in one direction or another may be present in many organs even though the most of them have not yet been isolated in pure form. F. Schultze (14), pursuing this idea, was able to obtain a marked increase in the polymorphonuclears with diminution of the mononuclears and eosinophiles by the injection of pressed spleen juice. He believes it may be concluded from these experiments that after destruction of the spleen, there is a preponderance of substances which act on the autonomic nerves; or as Bayer puts it in his iron metabolism studies, a paralysing autonomic hormone is absent (15). Subsequently, this internal secretory function is presumably taken over by the lymph nodes after which the blood picture returns to normal. Although

this theory is tempting on account of its simplicity, it must nevertheless be examined very carefully. It is, of course, not improbable that the normal blood picture is maintained by an equilibrium of the various internal secretions, but it must not be forgotten that our actual knowledge of the details in this field is still very meager. Very peculiar, and difficult to interpret, are the findings of Danilewsky and Selensky (16) who observed a marked increase in erythrocytes and hemoglobin after the injection of spleen and bone-marrow infusions even when the tissues had been previously boiled. On the strength of these results, attempts were made to improve severe anemias by administering "Lienin Pohl" and other preparations of spleen.

With the exception of these deficiency symptoms after splenectomy, our knowledge of the role of the spleen in blood regeneration and destruction is based especially on *morphological studies*. We know (17) that in embryonal life the splenic pulp shows erythropoetic masses but these never acquire the importance of those in the liver, but disappear before the embryonal period is concluded. The normal human spleen shows no such erythropoetic masses, but they have often been observed under pathological conditions, such as severe anemias, even post-hemorrhagic; bone marrow carcinomata, and various infectious diseases such as small pox, diphtheria, malaria and syphilis. The erythropoetic foci are always found in the pulp and never in the purely lymphatic Malpighian follicles. The latter are concerned with the formation of lymphocytes in embryonal as well as in adult life. Myelocytes are also developed in the pulp of embryonal spleen, and this also points to a close relationship with the bone marrow. In adults, the pulp consists of cells whose function is still in doubt and while it normally gives rise to no myelocytes, it retains the ability to produce them under pathological conditions. Thus a myeloid transformation of the splenic pulp is found in all sorts of infectious diseases; it can be produced experimentally, and finally it is often found in anemia and in tumors of the bone marrow.

More important than its function to *form blood corpuscles* is its ability to *destroy* them. This function also resides in the pulp in which large endothelial cells, the macrophages, take up and dissolve those red blood cells destined to destruction. If an increased breaking down of erythrocytes in the peripheral blood occurs from pathological causes, there arises a stimulus to the spleen; intense hyperemia of the organ develops, there results an hyperplasia of the cellular elements, and a splenic "tumor." This is also seen experimentally, first in blood intoxications, and second in infectious diseases, particularly those in which marked destruction of erythrocytes occurs (18). The substances liberated, especially the hemoglobin, are carried to the liver and there elaborated into biliary pigments,

with the exception of iron which is stored in the spleen. As we have already seen, if the destruction of red blood cells is too rapid, and the products are carried in too large a quantity to the liver, bile cylinders may be formed and lead to icterus. If the splenic function fails, the broken down red cells are taken up by the Kupfer's cells of the liver, and thus they act, so to speak, as a substitute for the spleen (19).

As stated above, the change in the blood picture after splenectomy, particularly the lymphocytosis and eosinophilia, must be considered as related to a stimulus which removal of the spleen produces not only on the lymph nodes and bone marrow, but also on a number of other organs which in their turn develop anatomical changes (20). Thus, as numerous writers have confirmed, there is swelling of the lymph nodes which renders about 20 per cent. of the superficial nodes enlarged to the touch (21). How often or how many of the deep lymph nodes are enlarged cannot of course be expressed in percentage, but according to autopsy records, the figure is quite high. In close histological relation to the lymph nodes are the so-called *hemolymph nodes* (22) which acquire a certain practical importance after splenectomy because they have often been confused with accessory spleens and have been described as such. These are structures which microscopically are identical with true lymph nodes, the only point of difference being that their sinuses contain blood. Because of this, they bear on superficial examination, a certain resemblance to splenic tissue and actually their function brings them in close relation to this organ since they contain erythrocytes and considerable amounts of the products of their destruction. Transitions into actual splenic tissue have, however, not been observed thus far. These hemolymph nodes also hypertrophy very markedly after splenectomy, and appear scattered in the mesentery as firm, dark red nodules, about the size of a finger nail, and grossly show great similarity to accessory spleens (23). All reports of the appearance of numerous accessory spleens after splenectomy must therefore be accepted with great caution.

V. Stubenrauch (24), who terms these spleen-like bodies "splenoids," thinks like Beneke, that they are from an implantation of torn and crushed spleen pulp. The experiments which he performed on the transplantation of splenic fragments showed, as a matter of fact, that these particles healed very well and were preserved for considerable time. Kreuter (25) also, on the basis of his experiments on monkeys, believes that the brownish nodules appearing in the peritoneum after splenectomy, are implants from liberated pulp. Cases similar to those of v. Stubenrauch have also been observed by others (26). Numerous (about 400) accessory spleens were discovered by Albrecht (27) in an individual who had not been splenectomized.

The oft cited statement of Giesker and Rosenmuller that accessory spleens are found at autopsy in 94 per cent. of southern Europeans and only once in every 400 northern Europeans and that this is related to the incidence of malaria in the former should be rigidly reinvestigated. In my experience, accessory spleens are found more often at autopsies in the north of Germany and other malaria free districts, than the published reports would indicate.

After partial removal, the spleen is able to *regenerate* extensively. This occurs not only in lower animals such as frogs (Eberhard, cited by Vulpus) but also in mammals as shown in an experiment of Laudenbach (28) on dogs, and an observation on a human case by Kuttner (29). In the latter, four years after almost total splenectomy for traumatic rupture, a spleen the size of a peach was found. When the blood changes after splenectomy pass over very quickly, it has always been related to such regeneration or to the presence of accessory spleens. Whether this is correct or not, can naturally be determined but seldom.

Of the other organs which are influenced by splenectomy, the *bone marrow* must be mentioned especially. As Mosler (20) first described, there are found hyperemia, active mitotic figures and increase in number of specific marrow cells with diminution in the amount of fat. The pressure of the increasing bone marrow leads to absorption of bone bridges which is evidenced clinically by gnawing pain in the long bones (Lohlein, cited by Vulpus), and also in a disturbance of ossification, although the latter is not always present. There are also occasional references to poor healing in fractures after splenectomy (Notzel cited by Meyer (1), (20), (30), (31)).

An *hyperplasia of the thymus* has also been found, and Bayer (15) believes from his investigations on iron metabolism after splenectomy, that the thymus acts vicariously for the spleen (32). But v. Braunschweig (32) found no changes in the thymus under these conditions. Vulpus (7) describes *swelling of the liver* and many describe *swelling of the thyroid* (33) but it is very difficult to interpret these changes physiologically at the present time; they are not found consistently so that they may only be chance results of the splenectomy. A certain satisfaction attends the use of the above mentioned theory of Schulze and Bayer that there is failure of a paralysing hormone acting on the autonomic system. Many of the changes described may be explained as a vagotonisation following this. It would also explain why all patients do not react to splenectomy with organic changes, but only those, if it may be so expressed, who have a particularly sensitive autonomic system. This applies especially to swelling of the thyroid. It is too elementary and meaningless to speak of the swelling of certain organs after splenectomy as "vicarious" manifestations. In



some cases the changes are probably only a result of the general operative shock. Thus a suddenly appearing Graves disease is occasionally seen after other severe operations, and, therefore, this condition is not characteristic of splenectomy and indeed it does not occur more often after this operation than after other laparotomies.

The part which the spleen plays in *iron metabolism* is very important. Asher (34) found that the elimination of iron is considerably increased in splenectomized dogs. M. B. Schmidt (35) showed experimentally that the iron in the spleen is derived principally from destroyed erythrocytes and tissue cells, and that contained in the food is stored chiefly in the liver so that the spleen retains most of its contained iron even on an iron-free diet. A large part of this ultimately reaches the liver which thus "assists" the spleen. Whether other organs, *e.g.*, the bone marrow, are also supplied with this stored iron to manufacture new red blood cells is not known with certainty. The results of Asher have been confirmed in humans by Bayer (36) who demonstrated an increased output of iron in several splenectomized patients. After splenectomy, the liver acts vicariously for the spleen, and assumes the storage of iron, but it is unable to hold it as tightly, and the hemoglobin of the blood diminishes, as Bayer found, after splenectomy during pregnancy. Lepehne (19) also demonstrated this increased output of iron by histological methods. [This disturbance in iron metabolism may, however, be a manifestation of increased blood destruction and not directly dependent on absence of the spleen.]

We have thus far examined the functions of the spleen only from the standpoint of its importance in the blood picture. A further function is manifested in *infectious diseases*. It is able to ingest any bacteria which are circulating in the blood and destroy them in a manner similar to the destruction of functionless red blood corpuscles. This is one way in which the spleen helps in the struggle against infection. It may, however, set free bacterial antibodies from the remains of white blood corpuscles. Naturally, many experiments have been undertaken to discover if splenectomized animals are less resistant to infection, and a number of writers (Ludakewitsch, see the contrary, Piktin (37), Bardoch (37), anthrax) believe there is both increased susceptibility to infection and decreased resistance. But when one after the other of the inherent experimental errors in such investigations had been overcome, more and more writers reached the opinion, that a splenectomized animal, if it were otherwise in good condition, shows no increased susceptibility. After splenectomy, as in every operative removal of an entire large organ, an animal is necessarily in a weakened condition and therefore any infection is more likely to be virulent. This lowered resistance however is not greater than after any other severe operation and is therefore not specific of splenectomy (Melni-

low (38)). When the large number of factors concerned in an infection is considered, it is easily understood that a very large number of experiments, and marked differences in the results are necessary before conclusions which will withstand criticism can be drawn. Investigations of the bactericidal power of the blood serum, before and after splenectomy, are much more enlightening in this problem. Thus Montuori (38) found that the blood of splenectomized animals showed a diminished bactericidal power which lasted from 20 days to 4 months after the operation. Here also, it must be remarked, that loss of blood and operative shock alone can diminish the natural antibodies of the serum (normal agglutinins (39)). Perez (9), on the other hand, could not demonstrate any change in the bactericidal and agglutinative power of the blood serum in a case in which he had removed a wandering spleen. Indeed there was even a slight increase in these powers. The practitioner is of course particularly interested in the resistance of splenectomized patients to infectious diseases and to sum up, it may be accepted that no positive influence was detected in any of the cases thus far described (Vulpius (7)).

It is well known that the spleen is usually spared from *metastases of tumors*. This is spoken of as a sort of tumor immunity and it has been the subject of much study with mouse tumors. Oser and Pribrom (40) believe they could show that the sarcomata of rats grew more quickly after extirpation of the spleen, but nothing is known of anything similar in man (lit. see Schmincke (41)).

What part the *spleen plays in digestion* is not definitely known. Gross (42) demonstrated a diminution in the pepsin of the gastric juice after splenectomy in a patient in whom it had been normal before the operation. Luciani (43) also states that the digestive power of the gastric juice is constantly diminished after extirpation of the spleen. This has been demonstrated in animals by Tarulli and Pascucci (44) and after the injection of extracts of spleen, this digestive power returned to normal. The old idea that spleenless individuals were possessed of large appetites was investigated by Richet (45) and he actually found, that for the same body weight, splenectomized dogs consumed more food in a day than normals. It would seem after these experiments and observations that the spleen does have some sort of influence on metabolism and the utilization of food. Further studies have led to the statement that splenectomized dogs have a reduced capacity for the assimilation of glucose, levulose and lactose, Quarta (1), but just how this occurs has not been demonstrated. It has been assumed that the spleen regulates the blood supply of the digestive organs and this conclusion has been drawn from several facts. As Schonfeld (46) has shown, first, the volume of the spleen is greatest during the time of digestion, second, contractile elements have been

demonstrated in the spleen, and finally Roy (47) detected rhythmic changes in splenic volume which occurred about every 60 seconds, and were independent of the fluctuations of blood pressure. The idea has been expressed in this way; the spleen acts as a "heart" for the portal system. But this regulation of blood supply can not alone explain the changes in digestive power, so an internal secretory power is suspected, but nothing definite in this direction has been discovered. Furthermore, the spleen has an influence on the motility of the intestines. As the animal experiments and the compilations of A. Meyer show (1) there often occurs a passing paralysis of the intestines with meteorism after splenectomy, but without other signs of peritonitis. Is this really more severe than after other operations? There are not sufficient records of prolonged constipation after splenectomy to answer this positively, even though it is said to have been observed. In opposition to these statements, Bayer (36) saw an increased activity of the intestines which he correlates with his theory of increased vagus tonus. Whether the splenic extract which Zulzer used therapeutically under the name of "Hormonal" owes its unquestioned ability to stimulate peristalsis to a hormone or only to a lowering of blood pressure on account of its content of "vasodilation" (Popielski, 48) has not been determined. At any rate it should not be concluded that the spleen is an especially important central organ for normal intestinal motility just because stimulation of peristalsis has been observed after the intravenous injection of "Hormonal." At present, observations such as those of Soulie (1) in which a long lasting constipation was relieved by splitting the capsule of an enlarged spleen, must be evaluated very cautiously.

Still more hazy is the importance of the spleen in *psychic processes*. Pohl (49) describes a case in which there was increased somnolence after splenectomy. Czerny (20) also observed nervous disturbances after the same operation.

When one other fact is added, we will have completed the enumeration of the known symptoms and conditions which appear after splenectomy. In very young animals, there is an increase in the *ash of their bodies* which is chiefly from increased calcium and phosphorus, although there is relatively less of the latter (2).

When the animals of Malassez and Pouchet (50) were bled a second time after splenectomy, the blood picture was apparently not altered, but others (51) believe that the usual symptoms are intensified by such a procedure although the latter do not give the details of their experimental results.

A pathologically increased *destruction of erythrocytes* in the spleen is the crux of the situation in a number of diseases in which a *severe anemia*

occurs (52). These diseases among which are hemolytic jaundice, pernicious anemia and Banti's disease are often successfully treated by splenectomy. Their etiology and possibly that of a few others belonging to the same group is not known, nor are we entirely positive that different types of one and the same disease are not given separate names. We can only say with our present knowledge, that the spleen is fundamentally at fault, and with its removal, a large number of patients with these diseases may be cured or considerably improved. Eppinger draws an analogy between a number of loosely connected diseases formerly grouped under splenomegaly, and the hyperthyroidism in Basedow's disease, justifying the comparison on the basis of therapeutic results.

*Jaundice* is a symptom frequently present in all these diseases and as we have already seen, it is a result of bile cylinder obstruction in the capillaries of the liver. The primary cause is a pathological hemolysis in the spleen. This can be imitated experimentally by administering toluendiamin to dogs. Banti (53) and Ivanovicz showed that it is more difficult to produce jaundice in splenectomized dogs with this substance than in normals, and the bile remains fluid in the former while it becomes viscid and dark from the extensive hemolysis in the latter. Therefore, we may conclude that the increased hemolysis is bound up with the presence of the spleen and it is only when the spleen participates in some manner that the toluendiamin becomes hemolytic. An approximate index of the degree of hemolysis can be obtained by estimations of the amount of urobilin in the stools. Eppinger and Charnass found a considerable increase in this substance in hemolytic icterus and in pernicious anemia. The conclusion is drawn quite correctly, that there is not insufficient formation of erythrocytes but an increased destruction of them in these diseases.

The relation of pathological conditions in the spleen to *diseases of the liver* has been the object of much experimental investigation (54). Mallory, and later Breccia, demonstrated inflammatory and necrotic foci in the liver after such injuries to the spleen as crushing, heating, electrolysis etc. Foa injected tubercle bacilli under the capsule of the spleen and then found miliary tubercles in the liver which healed after removal of the spleen. Such foci in the liver were also obtained when the splenic vein had previously been ligated, although in this case, the anatomical picture was somewhat milder. Conversely, the injection of tubercle bacilli into the liver resulted in a severe infection of the spleen. It must be concluded from such experiments that the liver and spleen are in very close relation through their lymph and blood supplies, and that diseases affecting the one organ readily make themselves felt in the other.



In these diseases, the bone marrow is driven to supply sufficient red blood cells to compensate the enormous diminution. In hemolytic jaundice it succeeds very well; the blood picture remains fairly normal, but in true pernicious anemia all sorts of immature forms, nucleated corpuscles etc. are thrown into the peripheral blood. As an additional factor in this compensation for the loss of blood, the connective tissue proliferation in the spleen as it occurs in the classical Banti's disease, should be regarded as an effort on the part of the organism at recovery (Eppinger).

Even though the view that these hemolytic diseases may be regarded as an "hypersplenism" is in many ways open to criticism and has not been sufficiently substantiated in all its details, it has the big advantage of offering a starting point from which this difficult question can be viewed from common ground (55). Surgically at least, it is not necessary to deal with single types, usually named after their authors, but with a disease pathologically physiologically uniform and one which can be characterized briefly as increased hemolysis brought about by an alteration in the spleen. If the spleen is removed in these cases, the hemolysis ceases, and in the most favorable cases, especially those in which secondary changes have not progressed too far, the disease is completely cured.

Approached from this standpoint, the etiology is of course entirely ignored. But it may be different in the various types, or, on the other hand, it may be but different degrees of one and the same process. The search for bacteria has been constant, particularly in Banti's disease, and especially by Banti himself, who believes in an infectious origin, but up until now observations either by cultures or by inoculation have led to no positive results. In contradistinction to those writers who believe in a single bacterial or toxic cause, others believe that they result from a summation of injuries, especially previous infectious diseases, which have damaged the spleen. Perhaps in addition there is a congenital weakness of this organ (Banti's disease of infantilism (56)). In connection with iron metabolism in Banti's disease, Bayer (36) found considerable retention of this substance in one individual and since there was also a lowered hemoglobin, he concludes, probably correctly, that the spleen of this patient could not supply its contained iron to the body as it was needed. The fact that an injection of adrenalin does not lead to an increase in white blood corpuscles in Banti's disease as it does normally, is often cited as another indication that there is dysfunction of the spleen in this disease (57). Investigations of Blumenfeldt (58) have shown that this is not always true, for a leucocytosis did occur when he injected adrenalin into a splenectomized individual. This reaction is therefore not dependent on the spleen.

*Injuries of the spleen* and their results deserve short mention, since they have led to many experimental studies. In the mechanism of tearing wounds there are a number of factors which interact, but no one in particular should be especially emphasized. The soft consistency of the organ, Berger (59) states, makes it possible to compare it to a bladder filled with fluid and to apply Pascal's laws according to which any pressure which is applied will spread equally in all directions. Investigations of Kon (60), however, have shown that the analogy is not fortunate because, while in any ordinary bladder, the pressure will spread equally, in the spleen, the capsule is less resistant to longitudinal than to transverse stretching. The reason for this is not known, but in all probability it explains why the great majority of tears of the spleen are transverse. A factor, leading to another limitation of Pascal's law, is that the spleen is not freely movable but is more or less fixed in its position by fairly strong bands. A large number of the cases of rupture must therefore be regarded as tearing-off fractures, a view which has much justification in those cases resulting from indirect force such as the one of Waldeyer reported by Brogsitter (21). In direct trauma, the importance of the fixation bands of the spleen lies principally in their causing it to become bent on its convex surface while holding it fixed in position and therefore preventing it from turning aside (61). But in these bending tears, much depends also on which part of the spleen is lying on the structures beneath. This is usually the side endangered, as the experiments of Kon have shown, and the various positions of the spleen depend principally on the amount of contents in the stomach and intestines.

If anhematogenous infection is engrafted on a splenic injury, it may lead to a sequestration of various portions, or even of the entire organ. In animals, Kuttner (62) could readily obtain such a splenic sequestrum by manual crushing of the organ followed by the injection of staphylococci into the ear vein.

#### LITERATURE TO SPLEEN

1. Lit. see coll. ref. by A. Meyer: Zentralblatt f. d. Grenzgebiete, 1914, Vol. 18, Hirshfeld, Deutsche Med. Wochenschrift, 1915, Schmincke, Munchener Med. Wochenschr., 1916.
2. Droge: "Einfluss der Milzextirpation auf die Chemische Konstitution des Tierkoerpers," Pfluger's Arch., 1913, 152, p. 437; Pfluger's Arch., 1914, 157, 486-500.
3. Lieblein, V.: "Ueber Magen-Darmblutungen nach Milzextirpation, zugleich ein Beitrag zur Kasuistik der isolierten Schussverletzungen der Milz," Mitth. a. d. Grenzgebieten, 1904, 17, 431-446.
4. L. Asher: "Die Funktion der Milz," Deutsche med. Wochenschrift, 1911, 37, p. 1252; Biochem. Zeitschft., 55, p. 13.
5. Vogel, H.: Biochem. Ztschft., 18, p. 386.
6. see Ehrlich: Die Anemia in Nothnagel's Handb, 1898, 8 (Lit.).

7. Vulpius: Brun's Beitrage, 1894, V. 11, p. 684.
8. Kuttner: Chirurgenkongress, 1907, p. 25.
9. Peres: 31 Jahresbericht f. chirurgie, 1907, 13.
10. Pearce, R. M., Krumbhaar, E. B., Frazier, C. H.: "The Spleen and Anemia," Lippincott Philadelphia, 1918.
11. W. Notzel: Brun's Beitrage, 1906, V. 48, 309-336.
12. Kreuter: "Experimentelle Untersuchungen ueber den Einfluss der Milzextirpation auf das periphere Blutbild," Arch. f. klin. Chirurgie, 1914, Vol. 106, p. 191.
13. G. Bertelle, W. Falta and O. Schweeger: "Ueber die Wechselwirkung der Drusen mit innerer Secretion." 3. "Ueber Chemotaxis," Zeitschft. f. Klin. Med., 1910, V. 71, p. 49.
14. Schultze, F.: "Beitrag zur Splenectomy bei der traumatischen Milzruptur und zur Frage der dadurch bedingten Blutveraenderungen," Bruns Beitrage, 1911, 74, p. 482.
15. R. Bayer: "Weitere Untersuchungen ueber die Funktion der Milz, vornehmlich ihre Rolle im Eisenstoffwechsel mit besonderer Berucksichtigung des Morbus Banti," Mitt. a. d. Grenzgebieten, 1913, 27, p. 311-340.
16. Danilewsky and Selensky: Pflugers Archiv., 1895, 61, p. 264.
17. see Naegeli: Blutkrankheiten, 1908, p. 72; Ehrlich, Die Anemia in Nothnagels Handb, 1898, 8, p. 56.
18. Jawein: Virchows Archiv., 1900, V. 161, p. 461.
19. G. Lepehne: "Experimentelle Untersuchungen ueber das Milzgewebe in der Leber. Ein Beitrag zum Hemoglobin-und Eisenstoffwechsel," Deutsche med. Wochenschrift., 1914, p. 1361.
20. Tizzoni: Arch. int. de Biol., 1882, 1, p. 34. Riegner: Berlin klin. Wochenschrift., 1893, p. 177. Mosler: Deutsche med. Wochenschrift., 1884, Vol. 22, p. 338. Czerny: Wiener med. Wochenschrift., 1879, p. 333.
21. Brogsitter, C. M.: "Splenectomie subkutane Milzruptur. Historisches, Kasuistisches und Kritisches," Charite-Annalen, 1909, p. 558.
22. Helly: Ergebn. d. Anat., 1902, V. 12, p. 207. Haberer: Arch. f. Anat. and Physiol., 1901, p. 47.
23. Mornadi and Sisto: cited by A. Meyer (1).
24. v. Stubenrauch: Chirurgenkongress, 1912, p. 214.
25. Kreuter: Zentralbl. f. Chir., 1919, p. 554.
26. Tizzoni: Arch. ital. de Biol., 1882, p. 36. R. Faltin: "Splenic formations in the peritoneum observed about 61½ years after splenectomy caused by rupture of the spleen," Deutsche Zeitschft. f. Chirurgie, 1911, 110, p. 160.
27. Albrecht: Zieglers Beitrage, z. pathol. Anat., 1896, 20, p. 513.
28. Laudenbach: Virchows Arch., 1895, V. 141.
29. Kuttner: cited by Stubenrauch, 24.
30. Laudenbach: Arch. de Physiol., 1896, 28, p. 706. Emelianoff: Arch. d. sciences biol. de St. Petersburg, 1893, V. 2, p. 135.
31. Elliot: New York med. Journ., 1907.
32. Klose, H. and Vogt, H.: "Klinik und Biologie der Thymusdruse mit besonderer Berucksichtigung ihrer Beziehungen zu Knochen-und Nervensystem," Bruns, Beitrage, 1910, V. 69, 1-200. v. Braunschweig: Inaug-Diss. Dorpat, 1891.
33. Winkler: Zentralbl. f. Chir., 1905, p. 257. Zesas: Arch. f. klin. Chir., 1885, V. 48 and 31. Metzger: Zeitschft. f. Geb. and Gynekol, 1890, V. 19, p. 31. Crede: Arch. f. Klin. Chirurgie, V. 28, p. 401. Tiedemann: Ztschft. f. Phys., 1833, V. 5.
34. Asher: Zentralbl. f. Physiol., V. 22.

35. Schmidt, M. B.: 15th Pathologentag., 1912, p. 91.
36. Bayer, R.: "Untersuchungen über den Eisenstoffwechsel nach der Splenectomie ein Beitrag zur Lehre von den Funktionen der Milz," *Mitth. a. d. Grenzgebieten*, V. 21, p. 338 and V. 27, p. 311.
37. Piktin: *Zentralbl. Bact.*, 15, p. 840. Ludakeevitsch: *Annales de l'inst. Pasteur* 1891, Vol. 5. Bardach: *Annales de L'inst. Past.*, 1891, V. 5, 1889, V. 3, p. 40.
38. Melnikow: Montuori: Referred to in *Centralbl. Bact.*, 1893, 13, 670.
39. Rost: *Inaug. Diss. Heidelberg*, 1908.
40. Oser und Pribram: *Zeitschft. f. exp. Pathol., Therapie*, V. 12.
41. Schmincke: *Lit. Munch. med. Wochenschrift*, 1916.
42. Gross, O.: "Ueber den Einfluss der Milz auf die Magenverdauung; Zugleich ein Beitrag zur Methodik der Pepsinuntersuchung," *Zeitschft. f. exp. Pathol. and Therapie*, 1910, V. 8, 169-180.
43. Luciani: *Lehrbuch der Physiol.*, V. 2, p. 152.
44. Tarulli and Pascucci: *Arch. ital. de Biol.*, 1901, V. 36, p. 188.
45. Richet: *Ref. Journ. de physiol.*, 1912, V. 14, p. 379.
46. Schoenfeld: *Inaug. Diss. Groningen*, 1855.
47. Roy: *Journ. of Physiol.*, 1882, V. 3, p. 203.
48. Popielski: "Die Theorie der Hormone und innere Sekretion," *Klinisch therap. Wochenschr.*, 1913, 20, p. 1134.
49. Pohl: *Deutsche Zeitschrift. f. Chirurgie*, 104, p. 196.
50. Malassez and Pouchet: *Compt. rend. Soc. de Biol.*, 1878.
51. Grunberg: *Inaug. Diss. Dorpat*, 1891, p. 58. Freiberg: *Inaug. Diss. Dorpat*, 1892. Eliasberg: *Inaug. Diss. Dorpat*, 1893, p. 23.
52. Eppinger, H. and Ranzi E.: "Ueber Splenectomie bei Bluterkrankungen," *Berl. Klin. Woch.*, 1893, u. *Natusf. Vers.*, 1913, Eppinger u. Ranzi *Mitt. a. d. Grenzgebieten*, 1914, V. 27, p. 796.
53. Banti: *Zieglers Beitr.*, 1898, V. 24.
54. Lit. s. Ziegler. in *Ergeb. d. Chir.*, 1914, V. 8, p. 683.
55. Turk: "Die Blutkrankheiten und deren chirurgische Behandlung," (Milzextirpation) *Deutsche Med. Wochenschrift.*, 1914, V. 13, 14, *Berl. Klin. Wochenschr.*, 1914, 51, 174. Muhsam, R.: "Die Blutkrankheiten und ihre chirurgische Behandlung," (Milzextirpation) *Deutsche Med. Wochenschrift.*, 1914, V. 13, 14. Mosse: *Naturforscherversammlung*, 1913 (surg. sect.). Decastello, H.: "Ueber den Einfluss der Milzextirpation auf die perniziöse anæmia," *Deutsche med. Wochenschrift.*, 1914, V. 13, 14.
56. Isaac: *Schmidt's Jahrb.*, 1912, 14, 315.
57. Frey and Lury: *Zeitschft. f. d. ges. exp. Medizin.*, V. 2 and 3.
58. Blumenfeldt: "Zur Frage der Funktionsprüfung der Milz beim Menschen," *Herlin. klin. Wochenschrift.*, 1918.
59. Berger: *Arch. f. Klin. Chir.*, 1907, 83.
60. Kon, J.: "Der Mechanismus und die pathologische Anatomie der subkutanen Verletzungen der Milz," *Vierteljahrsschrift. f. ger. Med.*, 1907, 34, 269-282.
61. Leverenz, Schoenwerth: Cited by Michelsson, *Ergebn. d. Chir.*, 1913, V. 6, p. 497.
62. Kuttner, H.: "Ueber sequestrierende Milzabscesse," *Beitrage z. klin. Chir. Tubing*, 1907. 54, 405-457. *Chirurgenkongress*, 1907, p. 23.



## CHAPTER VI

### THE PERITONEUM

Because of their development from the common cœlum, and because of their anatomical and physiological similarity in the sense of lining serous cavities, the peritoneum, pleura and pericardium have a large number of common physiological and pathological peculiarities. These will be discussed together in this chapter on the peritoneum.

The *serous coats* are made up of a thin layer of connective tissue covered by a single layer of flat epithelium, or endothelium, as it is now called. Of all the attempts to differentiate this endothelium from epithelium and classify it with the connective tissues that of Kolozoff and v. Brunn (1) who detected cilia on the surface of the serosa, seems to supply the best proof of the epithelial character of these cells.

[There is doubt that these projections were really cilia; possibly they were only artefacts such as tiny strands of fibrin. The term mesothelium has been suggested but in view of its long established usage, endothelium is probably to be preferred, especially so because of the doubt of the origin of the cells.]

But their functional properties are also indicative of this origin. Uninjured serous surfaces do not adhere (v. Brunn); it is only when the vitality of the cells is reduced that fibrin is poured out and *adhesions* develop which finally, by organization, become dense and tight (2). According to the view of Marchand and Ziegler, fibrin appears as an exudate of plasma from the surface vessels; but according to Neumann and Grawitz, its origin is a "fibrinoid degeneration of the uppermost layers and of the swollen cells of the surface" (cited by Heinz). The histological details in this question still give rise to differences of opinion (3). As in the skin, larger defects in the serosa are filled in, first by blood, and later by connective tissue; finally, endothelial cells grow in from the edges and cover the entire denuded area (4).

Peritoneal adhesions are not necessarily permanent, but may disappear. Ujeno (5) by using iodine solutions, produced abdominal adhesions in rabbits and after having assured himself of their presence by a second laparotomy, caused their disappearance by massage of the abdominal walls. The processes concerned in their removal consist of degeneration and absorption. New adhesions are prevented by the ingrowing covering

of endothelial cells which are found as tube-like islands in the zone of adhesions (v. Brunn). What part enzymic processes play in the solution of such adhesions is not known with certainty.

The histological processes in the course of the *encapsulation of foreign bodies* in the peritoneum have been studied by Monkeberg (6) who injected lycopodium into the abdominal cavity. The first change is degeneration of the endothelial cells and growth of surrounding connective tissue. The former cells then grow from the edges, and conditions return as close as possible to the normal. Thus the pathological anatomical course of the formation and disappearance of adhesions is fairly well understood. There are, however, a large number of physiological questions which require answers. For instance, it is not known whether the serosa of the abdominal, pleural and pericardial cavities, though embryologically similar, are equally subject to their formation. Lennander (7) believes that they are formed more readily in the peritoneum, while Burkhardt (8) thinks it is a case not of differing functions of the endothelium, but of mechanical changes. It is a fact that leucocytes may easily be obtained by light suction from the peritoneum but not from the pleura or pericardium. Since the preliminary step in the formation of adhesions is similar to the process of blood coagulation, the leucocytes are probably not unimportant as enzyme carriers. But the mere presence of blood in the peritoneum, does not favor the formation of adhesions for according to Schrunder (9), none developed even when the serosa was injured at the same time, but they did form very readily when microorganisms were added to the blood.

Since adhesions are, to say the least, unwelcome, all sorts of substances and methods which Payr (10) has catalogued, have been tried (experimentally, and in man) to prevent their formation. In general, two methods have been employed. The first consists of spreading certain smeary substances over the visceral and parietal surfaces of the peritoneum, and the second, of stimulating the intestines to vigorous peristalsis immediately after operation in order to prevent the formation of adhesions at the very start (11). Of the substances recommended for introduction into the abdominal cavity to prevent adhesions, mention may be made of olive oil, camphorated oil, liquid paraffin, gum arabic, gelatine, egg white, etc.; further, gold beater's skin, collodion, protective silk, etc., have been covered over the intestines (12). The results of all these experiments have been very meager. Some have believed that camphorated oil will inhibit them but others have recorded the opposite experience (13). It is of course necessary that an abdomen be reopened for adhesions in order that such cases may be evaluated. Of the other substances not one has stood the test of time.

[It must, of course, be remembered that the formation of adhesions is part of the process of normal repair, so that the problem is really not the prevention, but the limiting of adhesions to a point just consistent with repair.]

A particularly remarkable fact for surgeons to note is that *blood remains fluid in the serous cavities*, or to put it more cautiously, blood free in the peritoneal cavity is mostly encountered in a fluid or semifluid state. Many experiments have been performed to clear this question, but contradictory results were obtained.

The works of older writers (Brucke (14), Lister) may be ignored, since they were performed on cold blooded animals and cannot be applied directly to humans. Trousseau and Leblanc (15), drew blood from the jugular vein of a horse and injected it into its pleural cavity through a funnel. The blood coagulated immediately, serum was pressed out just as in a test tube and was absorbed in the course of a few days.

Extensive experiments were performed by Penzoldt (16), who allowed blood from one rabbit to pass through glass and rubber tubes into the pleural or peritoneal cavity of another rabbit. Examination for the coagulability of the blood was made either at autopsy or by puncture of the cavities. He found that there was always fluid blood present, even after nine days of hemothorax, but coagulation was also always found at the end of 24 hours. When blood was removed during the first two hours after its introduction, it was still fluid, but coagulation set in in vitro. On examination at later periods, coagulation did not occur until the fifth day, when it again set in but so slightly that Penzoldt concludes, probably correctly, that it was not true blood coagulation, but coagulation of a pleural exudate. He could demonstrate inflammatory processes in the pleura in practically every case.

When small amounts of blood were introduced into the abdominal cavity, no blood was found in three days, or perhaps only a few coagula. From this, Penzoldt concludes that the blood must have remained fluid for some time in the peritoneal cavity. Changes in the sense of a peritonitis were not demonstrable. This last point is of great interest for it is well known that hemorrhage into the abdomen, particularly in the upper abdomen (injuries to liver or spleen) gives rise to rigidity, and in fact, to all the clinical symptoms of peritonitis (Trendelenburg). This will be discussed later. It will also be shown that hemorrhage, in general, exerts a pronounced irritant effect on tissues, for blood out of its normal environment is certainly not an indifferent substance.

In work on the absorption of hemorrhage, Cordua (17) performed extensive experiments on the conditions occurring in intraperitoneal bleeding. He allowed the blood from the carotid artery of one dog to

flow through a tube into the abdominal cavity of another and by removing samples through fine glass cannulæ, studied its changes. Of course, this method yielded only approximate figures of the amount of blood which had coagulated and the amount which remained fluid, but the results are useful as they stand. Certain technical errors are inherent in all these experiments. As soon as blood has left the body and is no longer in contact with living tissue but flows through glass tubing, it becomes very unstable and coagulation begins very quickly (18). Furthermore, strict asepsis was not observed in the experiments cited. In addition, a large amount was introduced quickly, while in the hemorrhages in man, at least in those amenable to treatment, the blood pours in much more slowly. Finally, an animal's own blood and a foreign blood behave very differently, and this factor has not always been given sufficient consideration.

Nelaton (19) avoided a number of these errors, by attempting to produce hemothorax from stab wounds of the lung, but in other cases, he also used the injection method. The findings are thus briefly summarized in his publication; blood is coagulated in 24 hours at the latest, and serum is then pressed out. Therefore his results correspond in general to those of Trousseau. Riedel (20), who observed a very rapid absorption after injecting blood into the pleural cavity, also found that the largest part remained fluid and only a small part coagulated. After injection into a joint, he states that one-third coagulates and two-thirds remains fluid. The fluid portion of the blood is absorbed, the coagulated portion is first organized and then removed in this somewhat complicated way. Jaffe (21) believes that blood in joints first coagulates and later becomes fluid again. Pagenstecher (22) who led blood directly from the carotid artery into the pleural cavity of the same animal, found almost all the blood fluid during the first two hours, and after six hours there remained a non-coagulable fluid resembling blood with floating coagula.

Operative observations in hemorrhage into serous cavities, particularly the peritoneum, show that there is always a mixture of clots and fluid blood present. The relative quantities of each can only be judged. In slow hemorrhage, *e.g.*, secondary hemorrhage, there are more clots and less fluid; in rapid hemorrhage (rupture of liver or mesenteric hemorrhage) the findings are reversed.

From this synopsis it is evident that the writers on this subject have divergent opinions. The French say, coagulation in toto takes place; the clot expresses serum which is absorbed. Riedel and others find a rapid absorption without coagulation. Penzoldt and Pagenstecher occupy a middle position. These differences in results must depend on the methods, and the reason for the differences will be found only when it becomes known



why a certain part of the blood remains unclotted. In other words, chemico-physiological examinations are necessary to lead us further.

This question brings up a more general one; why *blood* which coagulates so quickly outside the body *remains fluid within the organism*. Roughly, this subject has undergone the following vicissitudes. Brucke's idea (23) is that there is some sort of a vital process of which we know nothing definite and the blood remains fluid only so long as the vessel wall is intact and living. Freund (24) believes that the absence of friction, that is, a pure physical process, is sufficient explanation. But the idea of slight friction is not entirely accepted and the "vital process" opinion is not excluded. It is known that there are present in the blood, coagulation producing and inhibiting substances, or at least their precursors (25) and that, *e.g.*, experimental injection of Witte's peptone (26) or tissue extracts (27) check coagulation. The opinion is therefore held at present that such substances are also important in maintaining fluidity of the blood in the living vessels. Indeed, it is held that in the final analysis, the coagulation or fluidity of the blood when brought in contact with animal tissues depends on the balance of these coagulation producing and inhibiting factors (28).

The view is often expressed that the same conditions which control the fluid state of blood in the vessels, also maintain its fluid character in the serous cavities. An antithrombotic property of the endothelium of the serosa has been spoken of but the thought has also occurred, that in addition to this, the blood may have been defibrinated by the movements of the lungs and diaphragm (Riedel). Without doubt a recent hemorrhage (about twenty-four hours old) must be sharply differentiated from the sanguinous fluid obtained at a later puncture. Many workers have experimented with fresh hemorrhage into the pleural cavity, in the light of newer opinions on blood coagulation (29). Israel produced hemorrhage by opening the internal mammary artery and found it could "not be antithrombotic substances, but only lack of fibrinogen which determined the absence of coagulation." Clotting was readily brought about by the addition of fibrinogen and when increasing amounts of completed thrombin were added, the coagulum of this mixture was as firm as that of the controls. If inhibitory substances had been present, the coagulum would necessarily have been less firm. Furthermore, no inhibitory substances could be extracted from the endothelium. But while Zahn and Chandler believed certain changes occurred in the fibrinogen of the blood on contact with the pleural endothelium, Henschen, Herzfeld and Klinger regarded the process entirely as one of "defibrination." The movements of the lungs, heart and abdominal organs whip out the fibrin just as it may be done with glass rods. The relative quantity of fluid and clotted blood, found at operation, either in the peritoneal, pleural or pericardial cavities, would therefore

depend entirely on the relative amount of movement which has been transmitted to the blood present. This opinion is supported by the finding of quantities of fibrin clots in such hemorrhages. In addition, it must not be forgotten that coagulation is further slowed by the very slight friction to which the blood is subjected in such serous cavities so that a less amount of agitation will lead to defibrination. That the movements of the intestines are not to be underestimated can be seen from the fact that air which has escaped from a partially covered perforation of the stomach is spread in small bubbles over the peritoneum. It would seem to indicate that a kind of "beating" of the air occurs.

The erythrocytes settle in the defibrinated fluid blood so that the fluid obtained by puncture of such old hemorrhages is poorer in hemoglobin and shows a diminution in the number of cells. These are gradually destroyed; numerous "shadow cells" appear and exudative processes are indicated by an increase in the number of leucocytes. These latter cells then predominate, so that paracentesis does not reveal a fluid hematoma, but an exudate (Ledderhose) which contains considerable mucoid material (30). Blood in a joint or serous cavity is therefore not an entirely innocuous substance and Bier has taken advantage of this fact to increase the formation of callous in pseudarthroses. But it does not of itself favor the formation of adhesions in the peritoneal cavity as the experiments of Schrunder (9) have shown. The pain in subcutaneous hemorrhage is considered by Pagenstecher as probably due to this tissue irritation. That the increased temperature, "absorption fever," is also an effect need only be briefly mentioned.

As already stated, hemorrhage into the abdominal cavity is a powerful irritant to the peritoneum and leads to peritoneal shock. The clinical picture in such intraperitoneal hemorrhage is apparently very serious. Actually, however, the danger from hemorrhage alone is often not very great (31). Even when patients appear exsanguinated after injuries to the liver or spleen, there may be found only a small amount of blood. Many gynecologists have recently become more conservative in their treatment of extra-uterine pregnancy.

According to the calculations of Wegner (32) the *total surface* of the visceral and parietal peritoneum in a moderately developed female is 17,182 sq. cm., while the total external body surface, according to the same author is 17,502 sq. cm. The surface of the peritoneum is therefore approximately as great as the total body surface and this explains the importance of the *absorptive and exudative processes* to the remainder of the body. Under the stimulus of this calculation, the absorptive and exudative processes of the peritoneum have been studied from the surgical viewpoint, by the most varied methods and under the most varied conditions.

Wegner, himself, injected measured amounts of saline solution and serum into the abdomen of rabbits, and after killing them at intervals, measured the amount of fluid remaining. As these experiments show, the absorptive ability of the peritoneum is quite astounding. Its rapidity has been calculated by injecting small quantities of solutions of various substances which can be readily detected in the urine. Among them were potassium iodid (33), lactose (34), salicylates or potassium ferrocyanide (Schnitzler and Ewald) and dye stuffs such as methylene blue. Since the time between injection and appearance in the urine is dependent on both the rate of absorption from the peritoneum and the excretory rate and power of the kidneys, such methods yield only relative results. When, therefore, excretion of iodine began in 15 to 20 minutes and lasted four to five hours, as in the experiments both of Schnitzler and Ewald and of Clairmont and Haberer, absorption of this substance must have occurred much earlier. This conclusion may safely be made by analogy with other salts which are eliminated more rapidly by the kidneys as for example, salicyl, which can be detected in the urine more quickly (Schnitzler and Ewald). As Wegner showed, the injection of potassium cyanide is followed by almost instant death, as though the poison had been injected directly into the blood stream. Absorption, therefore, is very rapid, but pathological conditions may alter the speed and furthermore, absorption does not proceed at the same rate during longer periods of time (35).

It is necessary now to study the *paths* by which soluble and insoluble substances leave the peritoneum. Dubar et Remy, Mafucci and Heusner (36) demonstrated that absorption takes place not only by way of the diaphragm, but also through the great omentum, the lateral ligament, Douglas's cul de sac, the gastrohepatic omentum, etc. Both lymphatics and blood vessels take part. Danielsen (37) found by examinations of thoracic duct lymph and of blood, that colloids are taken up by the lymph channels and crystalloids by the blood stream. Bacteria belong to the group of colloids. Insoluble particles, such as oil and milk droplets, blood cells, india ink, etc. pass into the lymphatics of the diaphragm and then enter the thoracic duct. These paths were described by v. Recklinghausen (38) in 1863 and the rich supply of this muscle is shown in the anatomical investigation of Kuttner (39). The question of stomata in the vessels, *i.e.*, clefts between the endothelial cells, whose presence was accepted by v. Recklinghausen, is also discussed by Kuttner, and they are proved to be absent (see also Muscatello (40)). The absorption of insoluble particles compared to that of fluids is relatively very slow. Oil and liquid paraffin can be found unabsorbed in the peritoneum even after 24 hours (41). In these studies and observations much depends, of course, on the position of the patient or the experimental animal, *i.e.*, whether the diaphragm



was at the lowest level or not. For, as Muscatello showed, the region of the diaphragm is the only part of the peritoneum from which insoluble particles are absorbed. Thus absorption from the peritoneum may be very considerably diminished if the patient is so placed that the chest and upper abdomen occupy a high position and the pelvis the lowest (Fowler's position). That solutions are also absorbed almost exclusively by the diaphragmatic peritoneum is shown by the experiments of Clairmont and Haberer in which they observed a very much delayed absorption of iodide solution after painting the under surface of the diaphragm with collodion. Substances tend to approach the diaphragm, as Muscatello and others have shown, not only on account of their weight, but also against the force of gravity. There is a current of fluid directed upwards, produced probably by the movements of the diaphragm and the intestines. The cause of this current is not entirely clear. At any rate, as v. Recklinghausen has already stated, up and down movements of the diaphragm, even in a dead animal, cause a more rapid taking up by its lymphatics, of particles scattered over its surface. A portion of the corpuscular elements are also first phagocytosed by wandering cells, and may be absorbed by omentum or mesenteries and thus be transported in the lymph channels (Metschnikoff (42)).

In contradistinction, fluids or true solutions enter the blood stream directly. Only a small quantity is carried away by the lymph. This can be demonstrated by pouring almost any dye solution into the abdomen and observing the lymph as it flows from a fistula of the thoracic duct. The urine is colored before the lymph (43) and even after the introduction of large quantities of saline solution into the abdominal cavity, no increase in the quantity of lymph from the thoracic duct can be observed (44). True solutions also are absorbed by the diaphragm. That this absorption of fluids is greatly dependent on the blood supply of the abdominal cavity is easily understood, since they enter the blood stream directly. A further demonstration of this point is afforded by the experiments of Klapp (45) who observed a greatly increased absorption after placing animals in a hot air chamber and producing an active hyperemia of the abdominal organs. Conversely, by producing venous stasis, Clairmont and Haberer demonstrated a diminished absorption. Cold applied to the abdomen diminishes absorption (37). Also, when the venous return is hindered by increased intra-abdominal pressure (*e.g.*, a large exudate) absorption is slowed. In such cases, the removal of a portion of the exudate relieves pressure on the veins; the return of blood is improved and the rate of absorption increases.

How do *pathological circumstances affect absorption*, especially from the peritoneum; what are the conditions after operative injury, inflammatory



processes, etc? (35). After simple laparotomy, absorption is slowed only a trifle, that is, the beginning of absorption is not delayed but it is found slowed if estimations are made over a longer length of time. If the intestines are pulled out of the abdominal cavity, the absorptive processes are much more disturbed, they begin very much later than normal but may be somewhat favored by moistening the intestines with warm saline solution. Anesthesia *per se* has no appreciable effect but a diminution of peristalsis produces diminution of absorption (Schnitzler and Ewald, Clairmont and Haberer). Clairmont and Haberer stimulated peristalsis with physostigmin and believed absorption in the rabbit began earlier. Schnitzler and Ewald could not observe an increased absorption by other methods, *e.g.*, tying off a low loop of bowel. Obviously the results obtained in experiments such as these depend much on the kind of animal used. The serosa of the rabbit is more sensitive than that of the dog. Much finer differences may, therefore, be obtained in the former animal. It is doubtful, however, if these particular experiments can be used as a basis for believing that the toxemia of peritonitis in man will actually be increased by the taking of food or cathartics (46).

According to Clairmont and Haberer, an inflamed peritoneum absorbs more quickly in the first stages of peritonitis, and later the rate is slowed. This decrease of the absorption rate in the beginning is particularly evident if the inflammation is brought about by chemical irritants. In bacterial peritonitis the increase is not so clearly seen. In the later stages, Schnitzler and Ewald, and Clairmont and Haberer found a decrease in the rate by the potassium iodide method, but Glimm, using milk sugar, could not demonstrate it. Likewise Peiser, by injecting bacteria into the abdominal cavity, first observed considerable absorption and then later only a very slight amount. The divergence of results in these animal experiments is not very difficult to explain. The gross anatomical pictures of the peritonitides are not similar throughout, because in one instance a large amount of exudate is poured out and a small amount in another. Furthermore, the amount of fibrin varies in the same way. It seems only natural that absorption experiments carried out with bacterial infection should lead to differing results.

A *chronic inflammation of the peritoneum* was produced by Schnitzler and Ewald by introducing mechanical irritants such as sand, glass, celluloid particles, etc. Wegner sought to produce the same result by repeatedly injecting air. These experiments showed that the chronically inflamed peritoneum absorbed less than the normal membrane; a result which agrees, as Schnitzler and Ewald emphasize, with the clinical experience, that sepsis occurs less readily from a peritoneum which is the seat of a chronic inflammation. It is well known, especially from experiments

of gynecologists, that the danger of a post-operative peritonitis may be diminished by previous injection of irritant substances such as camphor, oil, etc. (47). It may be mentioned that one or even many injections of air lead to no demonstrable anatomical change in the peritoneum.

Apparently, transudation into the peritoneum is not interfered with by either dry or moist eventration, but the amount of fluid which escapes in acute inflammation is often very large. Increased transudation, ascites, has been discussed under cirrhosis of the liver. According to the statements of Wegner (48) the fluid which is poured into the abdominal cavity after the introduction of glycerin or hypertonic salt solution may equal the body weight in 12 to 23 hours. In the acute forms of peritonitis, however, the fluid does not accumulate as in the chronic forms, because in the former condition, the absorptive processes are not delayed, so that during a given time interval almost as much will be absorbed as has been poured out. Furthermore, the experiments of Wegner ((48) p. 85) show that, normally, the peritoneum is able to absorb in from 12½ to 30 hours an amount of fluid equal to the body weight of the experimental animal, which coincides with what has been said of the exudative powers of the peritoneum. The formation of an exudate depends on an injury to vessel walls (Cohnheim). For information concerning the anatomical conditions in the endothelial cells during exudation, Borst's studies may be consulted (49). According to the investigation of Schrader (50) the injection of bacteria, dead or alive, or of bacterial filtrates leads to no increased transudation.

The *blood vessels* of the peritoneum and of the abdominal organs are innervated by the splanchnics which send fibres not only to the arteries but also to the portal system (51). This vascular bed supplied by the splanchnics, is an extraordinarily large one, and, therefore, this nerve has been called the "regulator of the general blood pressure." A dilatation of vessels in other parts of the body, *e.g.*, skin surface is quickly compensated by a slight constriction of those in the splanchnic area. The pressure in the aorta therefore remains stable but it falls considerably when paralysis of the vaso-constrictor fibres of the splanchnics develops, *e.g.*, in severe peritonitis. The individual is actually exsanguinated by bleeding into the vessels of his own abdomen. A good idea of the amount of blood which may be contained in these vessels can be obtained from an investigation of Mall (52). By stimulation of the splanchnic 3 to 27 per cent. of the blood in the portal system of a dog was driven into other vessels. This fall of blood pressure is one of the principal causes of death in peritonitis (see later). The details of the blood and lymph vessel supply of the peritoneum have been studied by Meisel (53). He found the visceral layers were far better supplied than the parietal, but both contained a very

rich capillary network which ramified in the loose sub-endothelial tissue. Before speaking of the sensory nerves of the abdominal organs, it may be useful to discuss briefly the *vegetative nervous system* in general (54).

It has been found, chiefly through pharmacological investigations, that it is advantageous to divide the nervous system supplying the organs which function involuntarily, into the sympathetic portion and the cranial, *i.e.*, sacral autonomic portion (55). This is a physiological, rather than an anatomical division, since anatomically, the entire vegetative nervous system shows similarities insofar as the fibres which lead outwards from the various parts of the brain, do not pass directly to their respective organs, but first enter groups of nerve cells, the so-called ganglia. Here, in all probability, they are completely freed from any influence of the will and then pass as independent nerve structures into the tissues they innervate. The activities of the ganglia are paralyzed by injections of nicotine (Langley) and the functions of the pre-ganglionic fibres may then be separated from those post-ganglionic.

When both the sympathetic and the cranial-sacral autonomic systems supply any organ, and most organs in the abdomen are so provided, their functions are to be regarded as antagonistic. If, for example, stimulation of the sympathetic leads to inhibition of the movements of the intestines, stimulation of the sacral autonomic or the abdominal vagus will lead to an increase of peristalsis.

At this place we must refresh our knowledge of the anatomy of the *sympathetic nervous system*. In spite of its special functional importance, the sympathetic is anatomically to be considered "only a part of the total peripheral nervous system which has become independent" (56). The visceral branches, which spring from each spinal ganglion cell, or more accurately, from the anterior root, represent a direct nerve supply to the viscera in lower animals (Petromyces). In higher animals this simple structure is complicated by the union of single rami viscerales (border strand of the sympathetic); by the addition of non-medullated fibres arriving from the periphery; and by the presence of ganglion cells along their course, which, in their development, represent displaced spinal ganglia, that is, the primitive centrifugal ramus visceralis and a few centripetal non-medullated fibres, is called in anatomy, the ramus communicans.

The largest, and from its function the most important of the ganglia in the abdomen is the *solar ganglion*, or, as it is also called, the *celiac plexus*. Its most important branches are the major and minor splanchnic nerves. It is not known with certainty whether the vagus merely traverses the plexus or if it is connected with the nerve cells. Since sensory, motor and vaso-motor fibres all enter the ganglion, its function is very complex and the clinical symptoms following its destruction or compression may there-



fore be very varied. Strehl (57) has collected the investigations on this subject which have been carried out up to the time of his article (1905). The experiments of Popielski (58) and Exner and Jager (59) have already been discussed. According to these, stimulation of the intestines after extirpation of the ganglion is said to be answered by a contraction lasting for a decidedly longer time. If the animals remained alive, they became emaciated and passed very foul smelling excrement. In agreement with these experimental results, Exner and Jager found strong spasms of the small intestines in a case of probable destruction of the solar ganglion. At autopsy there are found (Strehl) hemorrhages and ulcers in the mucosa of the stomach, duodenum and upper small intestines, dilatation of the vessels and hyperemia of all the abdominal organs, with enlargement of the liver, periodic occlusion of the common bile duct, transient glycosuria, albuminuria, acetonuria, and emaciation with general body weakness. Accordingly, therefore, the vaso-motor and motor centers for the intestines are probably located in the cœliac ganglion.

Strehl himself, however, did not observe changes in the mucosa of the intestinal tract following experimental extirpation of the plexus. The large glands seem to be little influenced by this operation but there have been no careful experiments done on this problem with fistula dogs. The only constant findings in the many experiments of a large number of workers, seem to be the accelerated emptying of the small intestines and the dilatation of the vessels supplying them.

The *sensitivity of the abdominal organs* has been much investigated from the surgical standpoint during the last few years, especially since the introduction and ever increasing use of local anesthesia (59). In speaking of this problem, a distinction must be made between mechanical stimuli and those impulses inherent in the organs themselves. The sensitivity to mechanical stimuli, such as cutting, crushing, sewing, etc. has been much studied, especially since the work of Lennander (77). Lennander and Wilms (61) were first of the opinion that only the parietal peritoneum was sensitive to pain, because they observed that patients experienced no discomfort when the intestine was sutured as in a resection, but manipulation of the parietal peritoneum was immediately painful as was also ligation of the mesentery. This observation was soon confirmed by Propping, Ritter (62) and many others, so that this point may be accepted as established. The part played by the nerves running along the blood vessels of the mesenteries is still evaluated differently by different workers. Lennander and Wilms held the view that these nerves in the mesentery, *i.e.*, in the visceral peritoneum, are less concerned in abdominal pain than the nerves in the parietal peritoneum and they therefore believe that abdominal pains of all kinds are produced by a



rubbing of the parietal peritoneal coats (Lennander) or by a "pulling" of the same membrane (Wilms). An actual inherent sensitivity of the intestines is denied by these writers solely on the basis of the results of their experimental investigations with mechanical stimuli. But the view of Nothnagel (63) must be more nearly correct; namely, that it is not entirely justifiable to compare the sensations which are obtained by mechanical stimulation of the bowel with those experienced when the organs are diseased. Newer work, such as that of Ritter, Propping, Kappis and others, also lays more stress on the pain nerves which traverse the mesenteries along with the vessels. A. W. Meyer (64) showed in animals that these sensory fibres reach from the mesenteric attachment approximately half way around the bowel, and the part of the intestine opposite this attachment could be gently distended with air or otherwise mechanically stimulated without eliciting pain. Naturally, such experiments can be of only border line value. It is not very probable, on the face of it, that these sensory branches end along a sharp line. It is better to assume that they become more sparse, so that there is a gradual diminution of sensation from the parietal peritoneum outwards to the intestine. The insensitiveness of the part of the bowel opposite the mesenteric attachment would then be only relative. This idea gains strength from the fact that the zones of sensation in the intestines vary widely in different species of animals. The intestine of man, for example, is distinctly less sensitive than that of the cat, which in its turn, is less sensitive than that of the dog (65). The presence of such individual differences is probably the reason a few writers (Ritter) have occasionally elicited pain in man by mechanical stimulation of the intestines.

Kast and Meltzer (66), as well as Ritter, found in their animals that the intestine is sensitive to pain. They believe that the opposing results of other writers are due to their methods, particularly to injury from the laparotomy. In surgical practice it can nevertheless be accepted that mechanical stimulation in general elicits pain only from the parietal peritoneum and from the mesentery, and that the pain from the latter is less in degree than that from the former. On this question there is a satisfying unanimity of opinion which is daily confirmed at operation.

But it is an entirely different question how non mechanical sensations, especially the pain in peritonitis, ileus, etc. are to be explained. As pointed out, a number of writers, like Wilms and Lennander, believe that all sensations in the organs of the abdominal cavity are initiated by pulling or pressure on the parietal peritoneum. When, as Wilms could show, a loop of small intestine is blown up with air, there is sufficient tension on the mesentery to produce a round hole when it is incised parallel to the

intestine. This makes it plausible that the pain of ileus is a pulling pain.

But not every pain in the abdomen can be explained in this way; there are many such sensations in the gastrointestinal tract, which cannot be considered due to a pulling of the organs. Lead colic, tabetic crises, pain of ulcer, and many others might be mentioned (67). In investigations of this subject, we are always confronted by the assumption that even if the abdominal organs are insensitive to cutting or puncturing or burning, they must be able to react with pain in certain kinds of diseases. The inherent sensitivity is attributed to the intestinal canal itself and not alone to the mesentery or the peritoneum. In addition, Nothnagel (63) states that "anemia is a stimulus sufficient to irritate the sensory nerves of the intestines; nerves which are otherwise insensitive to external stimuli," but at present this is not definitely proved, and is opposed by Lennander who could elicit no pain by producing anemia of the intestines with the Faradic current. On the other hand, the clinical observation that in arteriosclerosis of the mesenteric vessels, there is often severe abdominal pain (68), may be considered an argument in favor of the correctness of Nothnagel's views.

The *pain in ulcerative processes*, particularly gastric ulcers, is said by Kappis to be due to the direct irritative effect of the gastric juice on the nerves in the lesser omentum running toward its attachment to the intestines. This opinion is supported by Kappis, among other ways, by the injection of turpentine in the stomach wall. At first there is no pain but when the fluid has spread out and comes in contact with the roots of the greater or lesser omentum, the animal gives evidence of distress.

The tendency, therefore, of the later writers who have worked on this problem is to consider the sympathetic nerves which travel along the vessels particularly responsible for the inherent sensitivity of the viscera. As a matter of fact, this view is the natural one. Formerly, it was side-stepped only because it was taught in normal physiology that stimulation of the normal sympathetic did not elicit pain. The many experiments on this point have been critically reviewed in an admirable work by Buch (59). But now the investigations of Valentine, Brachet and others have actually shown that most severe pain is felt when the sympathetic or its ganglion is the site of an inflammatory change, as, for example, from exposure to the air for a time. It has therefore been argued that the experiments on mechanical stimulation of the intestines have not really shown what was intended, because no attention was paid to the damage done to the nerve by the laparotomy (66). As a result of this demonstration that an inflamed sympathetic is painful, we may at least admit the possibility that pain sensations in the abdominal viscera can be carried by

the sympathetic. In the final analysis, the whole question hinges on the fact that we are ignorant of the kind of stimulus to which the sympathetic responds with pain. May it not be possible that lead, when it produces its typical colic, not only stimulates the motor nerves of the intestines and causes spasm, but also irritates the sensory nerves in such a manner as to produce pain?

The paths through which these sensory stimuli reach the centers have been investigated after nerve section by a number of workers (69). Kocher (70) had already described cases in which after section of the spinal cord in the upper cervical and thoracic regions a diffuse peritonitis ran a painless course. The anatomical details of the course of the sympathetics and the splanchnics in the cord may be found in the papers of L. R. Muller (71). From the nerve sections of Kappis, it is probable that pain stimuli from the abdominal viscera are transmitted by way of the sympathetics and the splanchnics. Frohlich and Meyer after sectioning the spinal cord believe it is the spinal fibres which are concerned, a view which is opposed by v. Hoffman (72) and which also disagrees with the results of Kappis.

Finally, we do not know how the pain stimuli reach the centers of consciousness for we are not certain of the paths in the spinal cord which the sympathetic fibres traverse toward the brain. It has, however, been shown by the work of Head (73) that there is close contact in the gray matter of the cord between the sympathetic tracts coming from the viscera and the spinal sensory nerves from the skin. This is the reason for the extreme hypersensitiveness of the latter in many diseases of the viscera. The area of skin affected is supplied by sensory fibres from the same segment of the cord as that receiving the sympathetic rami communicantes from the diseased organ (see also the above remarks on the embryology). The best known instances are those occurring in injuries of the brain (74) and cardiac diseases, in which the hyperesthesias may often be extraordinarily severe, but they may also occur in renal and gastrointestinal diseases (75).

In view of all this, it must be said in summary that even if the pain from mechanical stimuli arises almost exclusively from the parietal peritoneum and mesentery, *i.e.*, indirectly, we are, nevertheless, capable of experiencing certain sensations from pathological processes in our viscera, by way of sympathetic nerves arising in the organs themselves. Lewandowsky also admits that the muscles supplied by the sympathetic system possess sensibility. He assumes that certain stimuli normally reach only the spinal cord, but when increased they may suddenly speed upwards and then be transmitted as pain to the periphery. He compares these processes to those in striated muscles from which we ordinarily do not

receive sensory impulses, but when an abnormally powerful contraction occurs, as in the calf, severe pain is experienced.

The proximal and distal ends of the intestinal tract, together with the bladder, have a separate innervation. This will be discussed under the particular organs (75).

The *innervation of the diaphragm* requires special mention because of the well known fact that pain in the shoulder and neck often occurs in affections of the upper abdomen, particularly in those around the diaphragm (76). The phrenic nerve which supplies the diaphragm carries both sensory and motor fibres. It should be mentioned, however, that according to the investigations of Ramstrom (77) it is only the more central portions of the diaphragm which are supplied on its peritoneal surface by the phrenic. The lateral parts are supplied by the sensory nerves of the abdominal wall. As Ohlecker (78) remarks, it should be assumed that there is a transmission of sensations in the spinal cord from the ganglion cells of the phrenic nerve to other sensory cells in the same segments (third to fifth) (see also 79).

The question of the functions of the **great omentum** has occupied the imagination and powers of observation of many investigators for years (80). Since it is known that an organ with no function atrophies and disappears, it is obvious that the great omentum has some duties to perform in the economy of the organism. Not only is it doubtful if all its functions are known, but in the interpretation of those that are, there is a great divergence of opinion. The fact that a fatty omentum protects the organs covered by it from cold is not to be disputed, but even if Aristotle, Galen, and others have considered this as the actual use of the organ, it can very well be objected, that a thick layer of fat in the abdominal wall would perform the same service (Bromann). This "function" alone therefore can hardly justify the existence of this organ.

The great omentum is not a fat reservoir, as the older writers believed (Bauhin, Hensing, Stosch, Glisson, and others), because its fat content usually parallels that of the rest of the body. Indeed it sometimes happens that an obese body has an omentum poor in fat (81), but we are unacquainted with the opposite condition. Still less explicable are the views of other authors that the function of the omentum is purely mechanical. Their ideas have been summed up in the catch word "plug" of the abdominal cavity (82) because it is frequently found in pathological bulgings of the abdomen, that is, in hernias. This fact in itself shows only the mobility of the organ and is evidence of those conditions which will be discussed under intraabdominal pressure. No striking "function" may be deduced from this, and just as little from the view that it guarantees the roundness of the small intestines and thus favors peristalsis (Fran-



sen). Attempts have often been made to construct a function from its anatomical position. Thus Heusner (83) recently reopened the whole question by stating that it acted as a support or anchor for the stomach and the colon. This view, expressed in such a form is not supported by fact, and it naturally provoked animated opposition (Witzel, Schiefferdecker, Gundermann (84), Bromann).

Fabricius ab Aquapendente regarded the great omentum as a reserve fold of the stomach. The latter organ folded itself between the leaves of the omentum so that when filled, it was partly covered with serosa belonging to the great omentum. This hypothesis is also mentioned by Cuvier. According to Bromann this could occur in the omentum only within 5 centimeters of the stomach. He observes that it is pure hypothesis to suppose that "our forefathers were such gluttons that they needed a reserve fold in the great omentum because of the tremendous dilatation of their stomachs." Gundermann (84) could not satisfy himself from animal experiments of the correctness of the belief that this folding occurred.

The view already advanced by Rivinus and Zigerus that the omentum is a regulator of the blood supply of the abdomen, has recently been revived by Witzel, Schiefferdecker and Gundermann, and Witzel believes that the bloody stools after resection of the omentum result from disturbed blood regulation. The ulcerations have already been discussed in connection with gastric ulcer and were related by v. Eiselberg (85), for instance, to retrograde embolism. Friedrich (86) observed multiple simple anemic and hemorrhagic necroses in the livers of guinea-pigs, which may be regarded as results of portal thromboses after resection of the omentum. According to the view of Gundermann such retrograde embolism points to an insufficiency of the valves in the veins of the great omentum. Since these valves are present in certain species of animals and absent in others, the varied experimental results might be explained by these anatomical peculiarities. The appearance of bloody stools, however, does not prove that the omentum regulates the blood supply if such hemorrhages are due to emboli. The same phenomenon has been described after extirpation of the spleen (see chapter on spleen).

Gundermann observed the vessels in the omentum of a dog after laparotomy both when the stomach was empty and when it was blown up by air, and believes he could see dilatation under the latter conditions. But the quantity of blood, which accumulates in the omentum, cannot be determined in such an experiment, and it is just this factor which must be known, if the function of blood regulator is to be assigned to the omentum. This view has not been proved by any means.

For the surgeon, the great importance of the omentum resides in its *protective power in infections*. It walls off the area of inflammation and

possibly helps in the destruction of organisms. The anatomical studies of Bromann have shown that the omentum first appears in mammals and that it must be regarded as a lymphatic apparatus. It is also known that it is particularly well developed in carnivora, and Bromann's explanation is the necessity for protection against the greater injury from splinters of bone contained in their food to the wall of the gastrointestinal tract with its resulting greater likelihood of peritonitis.

The first experimental investigation of the part played by the omentum in infection was done by Roger (87). He extirpated the organ of rabbits and guinea pigs and after a short time, injected cultures of staphylococci into their abdominal cavities. The animals died in two or three days while controls who received the same dose recovered completely. This showed that the great omentum is an important protection against infection, but gave no clue regarding the mechanism.

The absorptive process of the peritoneum has been discussed above from the general standpoint. The special work on that of the great omentum may now be added (88). If animals are killed a short time (15 minutes) after the injection into the abdominal cavity of carmine, india ink, or bacteria (Gundermann), it will be found that the diaphragm, especially the central tendon, is intensively stained, while the omentum will not as yet have taken up any of the dye stuff. If a longer time, 24 hours (Heusner, Koch), is allowed to elapse, the diaphragm will show less and the omentum will be deeply colored. The latter not only takes up dye particles and bacteria directly into its lymph channels, but also receives them from cellular elements (macrophages) which engulf the foreign particles and then wander back into its tissues. This may be termed indirect absorption (Koch) (for the origin of the phagocytic leucocytes in the abdominal cavity, see Weidenreich and Schott (89)). The lymph nodules of the omentum swell and become plainly visible during this taking up of bacteria. In chronic inflammations, *e.g.*, after experimental injections of tubercle bacilli in rabbits, the omentum becomes congested, swollen and rolled up in 24 to 48 hours, while otherwise the serosa is smooth and shiny. Whole parts of organs may also be taken up. Pirone (90) ligated the vessels of a rabbit's spleen and observed that the omentum wrapped itself around it and completely absorbed it in less than three weeks. Rost (91) observed a similar process around pancreatic tissue. As is well known, if pieces of pancreas are introduced into the abdominal cavity, the animals die of fat necrosis (see under pancreas). If, however, the pancreas is wrapped with omentum, its outline remains unchanged for weeks, but the tissue is completely destroyed and infiltrated with leucocytes (macrophages). In rupture of the liver, Suzucki (92) found liver cells and epithelium from the bile passages in the dilated lymphatics of the great omentum.

This organ is also an important part of the lymphatic apparatus of the gastrointestinal tract. Koch (88) by laparotomy introduced bovine tubercle bacilli into the intestines of rabbits and found that after several weeks, the omentum was covered with tubercles but the bowel mucosa was intact. Perhaps the staphylococci which Dudgeon and Roos found so frequently in perfectly healthy guinea pigs reached the omentum by the same route (93). Pirone (94) even believes that the omentum may function vicariously for the spleen, because after the injection of sodium taurocholate in normal animals, there is a marked "phagocytic reaction" in that organ, while in splenectomized animals, an hyperplasia of the lymph follicles in the great omentum appears. How far the omentum participates in the formation of antibodies has not been settled.

It has always seemed remarkable to surgeons how well the omentum is able to encapsulate inflammatory processes and to close peritoneal defects or ruptures of viscera. This property visualizes the importance of this structure as the protective organ of the abdominal cavity. It is found very frequently in hernial sacs. If the anterior abdominal wall is punctured by a bullet or stab wound, the omentum falls forward and closes the opening. If the appendix becomes the seat of inflammation, it is covered and protected by this "apron" and, at operation, it has often been found that the appendix has perforated into this protecting cavity. The abscess therefore remains localized and the remainder of the peritoneum shows no changes worth mentioning. Perforations of the bladder may also be plugged and closed in this manner (95). Many animal experiments relating to this have been performed (96) but they have only verified this well-known clinical observation of the activity of the omentum in encapsulating abscesses, etc. They give no information concerning the forces which bring the omentum to the point of danger. The idea of Morison that the omentum purposefully searches for these places is, of course, only an unproved assertion which was at once opposed by Beattie, Burn and Drummond. The omentum possesses no auto-motive power as Rubin showed (97), and clinical observations make it seem probable that the omentum encapsulates only when the endangered place is in its immediate vicinity. Thus it is found, for example, in experimental rupture of the bladder, that the omentum does not plug the opening in every case (Rost). But it is true that our knowledge of whether the omentum actually reaches areas of inflammation outside of its immediate vicinity is not certain. We know even less of the forces which could move it, but that mechanical factors are most important in determining the position of the omentum is shown in a communication by Kraske and by Bakes (98). The former describes a case in which an omentum weighty with fat, fell toward the diaphragm during a Trendelenburg position, and



caused the death of the patient. The latter observed in an equilibrist, whose performance consisted in walking about on his hands, that the omentum was covered over the liver and stomach and after the onset of an inflammation resembled a tumor.

Schiefferdecker believes that at first a thread of fibrin forms which shrinks and pulls the omentum but this is contradicted by the fact that even in the early stages of inflammation before the fibrin can shrink, the omentum covers the affected site. Aug. Mayer (99) believes a movement of the organs toward the omentum must be assumed, since, after its experimental removal he observed that perforations in the lower parts of the intestines reached a position under the remaining portion and were thus covered. Furthermore, it is known that increased peristalsis will displace the omentum and this is probably the most important factor in its movements. After all, it must not be forgotten that the omentum is very elastic, and is never really very far from the usual inflammatory foci—appendix, gall bladder, tubes, etc. and, therefore, the fact that the omentum is always at the right place need not greatly astonish us.

But it is remarkable that the omentum immediately becomes attached to any wound in the serosa and plasters over it. The mechanism of this property is still entirely unexplained. Even in free transplantations, it preserves its tendency of quickly adhering to underlying structures and forming a secure closure. In practical surgery, much use is made of this plastic property. Suspicious sutures of the intestines are covered by it; the stomach is covered by it to prevent displacement by adhesions after gall bladder operations; if in injuries of the liver, the hemorrhage cannot be controlled, a piece of omentum is sutured into the wound; in brief, these useful properties are called into daily surgical practice (100).

Especially astonishing are the experiments of Benker, Lanz and Rosenstein (101) designed to minimize the danger of gangrene after resections of the mesentery by wrapping the intestine with omentum. Lanz first separated the mesentery from its attachment to the bowel for a space of 5 cm., and then wrapped with omentum the segment of intestine which showed all the signs of nutritional disturbance. This operation was repeated a number of times on the same animal until finally as much as 50 cm. of small intestine was separated from its mesentery, and remained living. That the same thing can occur in man is shown by cases of Lanz and Rosenstein, but other operators were less fortunate (author's observation). At any rate, it does not seem advisable as has been suggested, to trust to the plastic power of the omentum, and not resect a portion of the colon when it is necessary to ligate the middle colic artery.

With all these important surgical properties of the omentum, it is clear that propositions such as that of Carlsson (102) to remove the omentum



in order to establish better drainage of the peritoneum, should not be entertained.

Occasionally *torsion of the omentum* with the clinical picture of intestinal gangrene occurs. Although this condition is rare, it is of general pathological interest, because studies of torsion of other abdominal organs have been stimulated by its occurrence (103). The process is presented most clearly in the omentum, but experiment and observation have shown that the causes even in this organ are multiple. In the first place, as Riedel pointed out, it occurs in hernias. The idea has been expressed that the omentum is forced into the hernial sac with a rotary movement, similar to that imparted to a bullet by a rifled barrel. But cases in which this state of affairs occurred are doubtless very rare. Other relations exist between a hernia and omental torsion which are probably of more importance. That portion of the omentum which finds its way into a hernial sac often shows inflammatory changes and becomes transformed into a mass of inflammatory tissue. In this manner, the specific gravity of separate portions varies and such differences in weight of the several parts of intraperitoneal organs are very important, as Payr points out. By the introduction of the metal magnesium into the abdominal cavity, he obtained cysts in the omentum filled with pure hydrogen, and later found spontaneous torsion of the organ in a number of his animals. It seems very likely that peristalsis played an active part in the production of this condition under those circumstances. In other experiments, torsion was found after sewing bits of cork, wood, paraffin, etc. into the omentum. Thus he could reproduce experimentally the same physical conditions which are present in "unequal growth" of the parts of a tumor, or in omental clumps.

According to Payr, another factor which favors torsion of an organ is the greater length of the veins as compared to the arteries. If stasis occurs, they stretch and twist, but the arteries remain the same in length. Payr could actually show by increasing the venous pressure in models and cadavers, that torsion of the omentum, as well as of a number of tumors, can be produced by such a "hemodynamic" method. This explanation is very plausible, especially in connection with torsions of the spermatic cord first described by Nicoladoni (104).

*Intraabdominal pressure* has been investigated by many authors and its importance was undoubtedly much overrated for a long time (105). It can easily be demonstrated by frozen sections of the abdomen that a free and empty space does not exist between the various organs. The atmospheric pressure resting on the yielding abdominal walls, equalizes pressure changes within the viscera by allowing the walls to contract or expand, as far as this is not regulated by more or less distention of the air

filled organs. The atmospheric pressure; in other words, the weight of the organs themselves, is therefore, as is really self evident, that which determines what has been called, somewhat obscurely, "intraabdominal pressure." The unequal weight of the viscera resting on the different parts of the abdomen must vary the pressure in the different parts of the abdominal cavity (Horrman). The pressure is less than atmospheric only in the region of the diaphragm, because here the elastic lungs exert a certain pull which, according to Kelling, is 8 cm. of water during expiration, and 40 cm. during inspiration. The viscera, therefore, show a tendency to rise in the abdominal cavity and in injuries to the diaphragm will enter the chest (diaphragmatic hernia). If the chest of a cadaver suspended in the upright position is opened, the diaphragm sinks downward and with it the viscera. But it must be remarked in this place, that we are not completely informed of the movements of the diaphragm during respiration.

Furthermore, if the abdominal organs are in such close contact without interspaces, it is reasonable that their relative positions are determined not only by the ligaments, etc. attached to them, but also by the fact that those organs above rest on those below, as on a cushion. Since the specific gravity of the viscera is about one, the pressure in the rectum equals the height of a column of water which reaches from the highest to the lowest points in the abdominal cavity. Generally speaking, the organs lie on each other, and, in the upright position, are from 2 to 3 cm. lower than in the prone position. This static pressure may also become negative, as for example, in the pelvic organs by elevating the pelvis, when air may enter the vagina, to escape on resuming the prone position ("garrulitas vulvæ"). Similarly, air occasionally enters the bladder during catheterization, and during operations in the elevated pelvic position, air is heard hissing into the abdominal cavity when the peritoneum is opened. According to Schreiber (106), a negative pressure occasionally occurs in the stomach, especially during attempts at inspiration with the glottis closed (Moritz).

Since the organs of the abdominal cavity are easily displaced during movements of the intestines, it is clear that those with the greater specific weight, liver, kidneys, filled stomach, etc. sink downward if there is a change in the tensions of the viscera from relaxation of the abdominal walls or of the pelvic musculature.

Like blood vessels, the hollow organs of the gastrointestinal tract have a certain pressure of their own, depending on the tonus of the musculature, which changes during peristalsis, etc. These varying pressures have been observed experimentally, when balloons were placed in different parts of the abdominal cavity (107). The development of this independent pressure is favored by the tension of the abdominal wall and this

in its turn appears originally because the walls grow more slowly than their contents.

It is not known with certainty if this independent pressure on and in the intestines has any relation to their function. Kelling (108) has shown that moderate filling of the intestines has no influence on their internal pressure, and that it rises only when the filling is quite considerable. It is therefore not necessary to forbid entirely the use of fluids after recent operations on the stomach, since moderate amounts do not endanger the sutures. This independent pressure has often been mistaken for "intraabdominal pressure" (Schatz) and this has led to much confusion.

According to Kelling, the pressure in the abdominal cavity is made up of the following factors:

1. Atmospheric pressure.
2. Static pressure.
3. Independent pressure of each organ.
4. Pressure changes from the action of abdominal muscles.
5. Pressure changes from respiration and heart beat.
6. Pressure on organs from the special position of the body.
7. Pathological pressure from overfilling of the abdominal cavity from a normal passive tension of the abdominal wall.

Ordinarily the abdominal walls exert no pressure on the viscera except when they are tightly contracted, and *vice versa*, their tension is increased by conditions such as ileus in which the pressure in the intestines is especially high. This will be referred to in speaking of ileus. The influence of respiration and heart beats need not be discussed. Slowly growing tumors, pregnancy, etc. do not lead to an increase of pressure because of the elasticity of the abdominal walls (Hormann (105), p. 553). Whether the "relaxation hyperemia" of which Wagner speaks is really due to removal of the pressure when the abdomen is opened, or whether it is due to the inflow of cooler air, is not as yet decided. Nor has it been definitely shown that the better results obtained in the treatment of peritonitis by closing the abdominal cavity to a small drain, are due to a re-established intraabdominal pressure (Notzel (31), Guleke (109)).

In the origin of *enteroptosis*, a special importance has been attached to this pressure (110). This is undoubtedly justified insofar as the separate factors concerned in pressure and tension are able to determine the position of the organs.

The purely mechanical factors in the production of *enteroptosis* are as follows:

1. General enlargement of the abdominal cavity. The *enteroptosis* in individuals with a pendulous abdomen is viewed by many surgeons

(111) as a special form (maternity enteroptosis) and is separated from other forms (virginal enteroptosis). Physiologically, such divisions are always somewhat arbitrary; but they serve a useful purpose. The importance of the abdominal walls in maintaining the relative position of the viscera may be illustrated under the fluoroscope not only in individuals with enteroptosis and lax abdominal walls, but in normals as well, by placing a well fitting abdominal binder in position, when the abdominal organs will be forced upwards (113).

Hernias and weakness of the muscles of the pelvic floor are of less importance. As a subdivision but more because of its historical interest, the view of Glenard (114) through whose work the whole problem of enteroptosis was brought to the front may be mentioned. He believed an emptiness, *i.e.*, shrinking of the bowel and with it of the entire abdominal contents, was especially important in the development of this disease. In general, however, an emptiness of the intestines points to a secondary and not a primary disease.

In contradistinction to general enlargement, a second mechanical condition in the origin of an enteroptosis is a diminution of one portion of the abdominal cavity, that is, of the hypochondrium. A low position of the diaphragm as it occurs in emphysema or tuberculosis (115) is accompanied in quite a large percentage of cases by splanchnoptosis even if only of mild degree. Thus Bial (116) found splanchnoptosis eighteen times in 26 cases of emphysema. According to the opinion of most writers, however, tight lacing either with a corset, skirt band, or belt is a more important factor in this particular type. Tight lacing, first, compresses the hypochondrium directly and secondly, it interferes with respiration by fixing the thorax, and this is also of importance in determining the position of the viscera.

These injurious mechanical factors just mentioned, unquestionably operate in a large number of individuals who show no sign of enteroptosis. There is a type of chest, long, narrow, and flat, with which a diminished capacity of the upper abdominal cavity is associated and which occurs without any kind of lacing. This has led to the opinion that the mechanical factors are only secondary influences in splanchnoptosis, and that the actual cause is a constitutional weakness of the tissues. Stiller (117) describes the "*habitus enteropticus*" as an individual with long flat chest, down hanging ribs, slightly pendulous abdomen, slight build, particularly of the skin and bones, potential hernias, tendency to flat feet; in brief, it is the type which was formerly characterized as "*phthisical*." There is undoubtedly a great deal of truth in this opinion that the mechanical factors are only secondary, and that constitutional weakness is the primary cause. But it must not be forgotten that it is actually in the "*habitus*



enteropticus" that all these mechanical conditions which favor descent of the viscera are present to their greatest degree.

The causes, therefore, of enteroptosis should be regarded first as tissue weakness, and second as mechanical, and these two may often be combined. In certain cases the constitutional cause is the more important; in others, *vice versa*. Just as the causative factors must be judged, so must the discomforts be considered from something more than a general viewpoint. Undoubtedly, pulling-pains or the sensation of weight in the abdomen can be explained by enteroptosis, but the symptoms are usually of a more general nature. In this connection, certain experiments of Emma Schulz (118) are of interest. Plethysmographic measurements of the arms of normals and of individuals with enteroptosis showed that, in the latter, there was no increase in the size of the arm after changes in the position of the body, perhaps because of venous stasis. A filling of the arm as in the normals, could, however, be obtained in the enteroptotics after lifting up the viscera.

In practice, and especially in treatment, the maternal and the virginal forms of enteroptosis have always been differentiated (see among others, Rovsing (111)). The mechanical factors will be credited with great importance only *cum grano salis*, in this type, *i.e.*, the enteroptosis with pendulous abdomen. Consequently an abdominal binder which supports the pendulous abdomen, will often work wonders, as will eventually perhaps an appropriate operation (119). In the virginal enteroptosis, on the contrary, there is usually a constitutional weakness at work, in which the ordinary treatment, fixation of single organs, only influences a symptom without curing the disease. The results of therapeutic measures must be viewed from this standpoint. A suitable interference is, to begin with, not unjustified, but it must be evaluated correctly.

For the development of *hernias* and for the positions of the abdominal organs, the firmness of the peritoneum, as well as the intraabdominal pressure is important. The first investigations in this field were performed by Scarpa (120). Moro (121) revived and amplified his experiments by testing the resistance of the peritoneum of dogs and cadavers to pneumatic pressure, both *in situ* and after excision. He found that the resistance of the parietal peritoneum in man is very high and exceeds in its mean, one atmospheric pressure. The elasticity is also very great, indeed almost absolute. Experimentally, the membrane tears before it is possible to overcome this elasticity. The resistance and elasticity of the peritoneum forming a hernial sac are even greater. It cannot, therefore, be accepted that a hernia enlarges through stretching of its sac, but either because it actually grows, or because additional peritoneum slides in from the abdominal cavity. This sliding of the peritoneum could not, it is true, be demon-

strated experimentally by increasing the intraabdominal pressure after dissecting free a piece of the membrane from the abdominal walls. But that such a process can occur under pathological conditions is shown by the so-called slide hernias. Evidently, in patients with this condition, the attachment of the peritoneum to its supporting structures is less firm than in the dogs used for these experiments. How often such a sliding of the peritoneum occurs in ordinary hernias is difficult to estimate. It can only be said that there are large hernias which develop very slowly (particularly umbilical hernias) in which the union of the hernial sac to the hernial opening is so firm that the possibility of a sliding can be excluded. The looseness and elasticity of the peritoneum is, in addition, a very considerable protection against infection as pointed out by Danielson (37). Extraperitoneal abscesses push the serosa forward, and do not usually perforate, and an empyema of the gall bladder may stretch the serosa covering it many times before perforation occurs.

Before the most important disease of the peritoneum—peritonitis—is discussed, the physiology and pathology of the intestinal tract must be considered.

#### LITERATURE TO PERITONEUM

1. Kolozoff und v. Brunn: Zieglers Beitrage, V. 30.
2. Vogel: Deutsche Zeitschft. f. Chir., 1902, V. 63, p. 296. Heinz: Virchows Arch., 1900, V. 160, p. 365. Graser: Deutsche Zeitschft. f. Chir., 1888, V. 27 and Arch. f. klin. Chir., 1895, V. 100, p. 887.
3. Muskatello: Munch. med. Wochenschrift., 1900, No. 20.
4. Marchand: Deutsche Chir., 1901, V. 16, p. 293. Burci: Lo sperimentale, 1903, No. 5.
5. Ujeno: Bruns Beitrage, 1909, V. 65, p. 277.
6. Monkeberg: Zieglers Beitrage, V. 34.
7. Lennander: Deutsche Ztschft. f. Chir., 1902, V. 63, p. 1.
8. Burkhardt: Arch. f. klin. Chir., 1917, V. 108, p. 399.
9. Peres: 31 Jahresbericht f. Chirurgie, 1907, 13. Schrunder: Inaug.-Diss. Heidelberg, 1914.
10. Payr: Naturforscherversammlung Wien, 1913.
11. Lawson Tait, Heidenhain, Vogel: Deutsche Zeitschft. f. Chir., V. 63.
12. Vogel-Busch-Bibergeil: Arch. f. klin. Chir., V. 87. Stern: Bruns Beitrage, 1889, V. 4. Lauenstein: Arch. f. klin. Chir., V. 45.
13. Hirschel: Munch. med. Wochenschrift, 1912.
14. Brucke: Virchows Arch., V. 12, p. 178.
15. Trausseau und Leblanc: Journ. de med. Veterinaire, Vol. 5, p. 104.
16. Penzoldt: Deutsches Arch. f. klin. Med., 1876, V. 18.
17. Cordua: Ueber d. Resorptionsmechanismus v. Blutgussen Preisschrift, Berlin. Hirschwald, 1877.
18. Ledderhose: Beitrage z. Kenntniss d. Verhaltens v. Blutergussen in seroesen Hohlen Strassburg, 1885.
19. Nelaton: Des epanchements de sang, These de Paris, 1880, p. 27.

20. Riedel: Deutsche Zeitschrft. f. Chir., 1880, 12, p. 447.
21. Jaffe: Arch. f. klin. Chir., 54, p. 90.
22. Pagenstecher: Bruns Beitrage, 1895, 13, p. 264.
23. Brucke: Virchows Arch., 1857, V. 12.
24. Freund: Jahrb. d. K. K. arztl. Ges. Wien, 1886.
25. Schmidt: Blutlehre F. C. W. Vogel, 1892.
26. Schmidt Mullheim: Arch. f. Anat. u. Physiol., 1880.
27. Naunyn: Arch. f. Pharmak., 1873, 1, p. 1.
28. See Freund in Marshand-Krehlschen: Handbuch d. allg. Pathol., V. 2, p. 32 ff.; also Beneke, in same book.
29. Israel: Mitt. a. d. Grenzgebieten, 1918, V. 30, p. 171. Zahn and Chandler: Biol. Ztschft., 1913, V. 58, p. 130. Herzfeld and Klinger: Bruns Beitr., 1916, 104, p. 196.
30. Pagenstecher: Mitt. a. d. Grenzgebiet, 1913, V. 25, p. 670.
31. Notzel: Bruns Beitrage, 1908, V. 61, p. 226.
32. Wegner: Arch. f. klin. Chir., 1877, V. 20, p. 64.
33. Schnitzler and Ewald: Deutsche Zeitschft. f. Chir., V. 41, p. 341. Clairmont and Haberer: Arch. f. klin. Chir., 1905, v. 76, p. 1.
34. Klapp: Mitt aus d. Grenzgebieten, 1902, V. 10, p. 254.
35. Feiser: Bruns Beitrage, 1906, V. 51.
36. Mafucci: Giornal internaz delle Scienze med., 1882. Dubar et Remy: Journ. de l'Anat. et. Phys., 1882, 18. Heusner: Munch. med. Wochenschft., 1905, p. 1130.
37. Danielsen: Bruns Beitrage, 1907, V. 54, p. 458.
38. v. Recklinghausen: Virchows Arch., 1863, V. 26, p. 172.
39. Kuttner: Bruns Beitrage, 1903, V. 40, p. 136.
40. Muscatello: Virchows Arch., 1895, V. 142, p. 327.
41. Hirschel: Bruns Beitrage, 1907, V. 56, p. 263. Glimm: Deutsche Zeitschft. f. Chir., V. 83, p. 254. Busch and Biebergeil: Arch. f. Klin. Chir., 1908, V. 87, p. 99.
42. Metschnikoff: In Kolle-Wassermanns Handbuch d. pathogenen Mikroorganism, V. 2, p. 1-704.
43. Starling und Tubby: Journ. of Physiol., 1894, V. 16, p. 140.
44. Orlow and Heidenhain: Pflugers Arch., 59. Heidenhain: Pflugers Arch., 1896, 62, p. 320.
45. Klapp: Deutsche Ztschft. f. Chir., 104, p. 535 and Mitt. aus d. Grenzgebieten, 18, p. 79.
46. Weil: Ergebn. d. Chir., 1911, 2, p. 295.
47. Hoehne: Munch. Med. Wochenschrift, 1909.
48. Wegner: Arch. f. klin. Chir., 1876, 20, p. 106.
49. Borst: Das Verhalten der Endothelien bei der acuten and chronischen Entzundung usw. Wurzburg, 1897.
50. Schrader: Deutsche Ztschft. f. Chir., 1903, V. 70, p. 421.
51. Pal: Jahrbucher der Wiener Aerzte, 1888. Schmid: Pflugers Arch., 1909, 126, 176-192.
52. Mall: Arch. f. Anat. u. Physiol., 1892, p. 419.
53. Meisel: Bruns Beitrage, 1903, V. 40.
54. Lewandowsky: Handbuch d. Neurologie, 1, p. 308-417.
55. Langley in Asher-Spiro: Ergebn. d. Physiol., 1903, V. 2, p. 808 and Meyer, Gottlieb: Exp. Pharmacol., 2, Ed. p. 126.
56. Gegenbaur: Lehrbuch d. Anat., 1899, 2, p. 523.

57. Strehl: Arch. f. Klin. Chir., 1905, V. 75, p. 726.
58. Popielski: Arch. f. Anat. and Phys., 1903, p. 338.
59. Neumann: Mitt. a. d. Grenzgebiete, 1910, V. 13. Kappis: Mitt. a. d. Grenzgebieten, 1913, V. 26. Exner and Jager: Mitt. aus d. Grenzgebieten, 1909, 20, p. 645. Buch: Arch. f. (Anat.) u. Physiol., 1901, 197.
60. Lennander: Zentralbl. f. Chir., 1901; Mitt. a. d. Grenzgebieten, V. 10, 15, 16; Deutschr Zeitschr f. Chir., 1904, V. 73.
61. Lennander und Wilms: Munch. med. Wochensch., 1904; Mitt. a. d. Grenzgebieten, V. 16; Deutsche Zeitschrift. f. Chir., 100; Med. Klinik, 1911, No. 1.
62. Ritter: Arch. f. klin. Chir., V. 90. Propping: Bruns Beitrage, V. 63.
63. Nothnagel: Arch. f. Verdauungskrankheiten, V. 11.
64. A. W. Meyer: Mittelrh. Chirurtag, July, 1914 Deutsche Zeitschft. f. Chir., 1919, V. 151.
65. Franke: Berliner Klin. Wochenscht., 1912, p. 1997. Engelhorn: Zeitschft. f. Geb. u. Gynak, 1911, V. 69, p. 66.
66. Kast und Meltzer: Mitt. a. d. Grenzgebieten, V. 19.
67. L. R. Miller: Mitt. a. d. Grenzgebieten, 1908, 18, No. 4, p. 614. Kuttner: Ueber abdominale Schmerzanfalle in Albus Sammlung zwangloser Abhandlungen aus dem Gebiete der Verdauungs. u. Stoffwechsel krankheiten, V. 1, No. 3.
68. Ortnr: v. Volkmanns Sammlung, No. 347.
69. Frohlich and Meyer: Wiener klin. Wochenscht., 1912, p. 29.
70. Kocher: Mitt. a. d. Grenzgebieten, 1896, V. 1.
71. L. R. Muller: Deutsche med. Wochenscht., 1911, Mitt. a. d. Grenzgebieten, 1908, V. 18. Arch. f. Klin. Med. 1911, V. 105.
72. V. Hoffmann: Mitt. a. d. Grenzgebieten, 1920.
73. Head: Die Sensibilitatsstorungen d. Haut bei Viszeralerkrankungen (August Hirschwald, 1898).
74. Wilms: Mitt. a. d. Grenzgebieten, 11, 697. Forderreuther: Ueber Headsche Zonen bei Viszeralerkrankungen Inaug. Diss. Heidelberg, 1913.
75. Zimmermann: Mitt. a. d. Grenzgebieten, V. 20, p. 445.
76. Nothnagels: Handbuch, V. 14, p. 570.
77. Ramstroem: Mitt. a. d. Grenzgebieten, 1906, V. 15, p. 642.
78. Ohlecker: Zentralbl. f. Chir., 1913, p. 852.
79. Hess: Munch. Med. Wochenscht., 1906.
80. Brohmann for lit.: Die Entwicklungsgeschichte d. Bursa omentalis usw. Wiesbaden., 1904. Bergman. Ders. Ergebn. d. Anat. u. Entwicklungsgeschichte, 1905, 15, p. 394. Ders. Hdbch. d. Audt. d. Mensch. v. Bardeleben, V. 6, 3, 2, p. 98.
81. Schiefferdecker: Deutsche med. Wochenscht., 1906, p. 988.
82. Fransen: Zeitschft. f. angeu Anat. u. Konstitutionslehre, 1914, V. 1, p. 258-268.
83. Heusner: Munch. Med. Wochenscht., 1905, p. 1130.
84. Gundermann: Brun's Beitrage, 1913, V. 84, p. 590.
85. v. Eiselberg: Arch. f. klin. Chir., V. 59.
86. Friedrich: Arch. f. klin. Chir., V. 61.
87. Roger: La semaine medicale, 1898, 18, p. 79.
88. Roser: Inaug. Diss. Strassburg, 1907. Koch: Med. Klinik., 1911, No. 51, and Zeitsch. f. Hyg., 1911, V. 69. Stuzer: Diss. Petersburg, 1913, Ref. Zentralbl. f. d. ges. Chir., 2, p. 635. Heger: Cited by Bromann.
89. Weidenreich: Anatomkongress 20th. Schott: Arch. f. mikroskp. Anatomie, 1909, V. 74.
90. Pirone: Arch. ital. Biol. F., 1903, 2, (Ref.)



91. Rost: Unpublished.
92. Suzucki: Virchows Arch., V. 202.
93. Dudgeon and Roos: Am. Journ. of Med. Sciences, V. 132, p. 37.
94. Pirone: Cited by Danielson, Bruns Beitrage, 54, p. 468.
95. Rost: Munch. Med. Wochenscht., 1917, No. 1. Cornil and Carnot: La semaine med., 1898.
96. Morison: Brit. med. Journ., 1906, p. 76-78. Enderlen: Deutsche Ztscht. f. Chir., V. 55.
97. Rubin: Surg. Gynec. and Obstetr., 1911, V. 12.
98. Kraske: Chirurgenkongress, 1904. Bakes: Arch. f. klin. Chir., 1904, V. 72, p. 70.
99. Aug. Mayer: Munch. med. Wochenscht., 1912, 59, p. 2497.
100. Hesse: Brun's Beitrage, 1, 82.
101. Rosenstein: Deutsch. Chirurgenkongress, 1909, 1, p. 172. Benker: Inaug. Diss. Heidelberg, 1893.
102. Carlsson: cited in Hygiea, 1898.
103. Payr: Arch. f. klin. Chir., 1902, V. 68. Deutsche Zeitscht. f. Chir., V. 85, p. 392. Pretsch: Bruns Beitrage, V. 48. Riedel: Munch. Med. Wochenscht., 1905. Hadda: Bruns Beitrage, V. 48. Lit. see Hochenegg. Wiener klin. Wochenscht., 1900, p. 291. Finsterer: Bruns Beitrage, V. 68.
104. Nicoladoni: Arch. f. klin. Chir., V. 31.
105. Weisker: Schmidts Jahrbucher, V. 219, p. 277. Moritz: Zeitscht. f. Biologie, 1895, V. 32. R. Meyer: Zentralbl. f. Gyn., 1902. Schatz: Verh. d. Deutsch. Gesellsch. f. Gyn., 4. Kongress Leipzig, 1892, 173. Kelling: v. Volkmanns Sammlunz klin. Vortrage No. 44. Hormann: Arch. f. Gyn., 1905, p. 527 (lit.)
106. Schreiber: Deutsch. Arch. f. klin. Med., 1883, V. 33.
107. Kertecz: Deutsche Med. Wochenscht., 1903, and Berlin klin. Wochenscht., 1904.
108. Kellung: Arch. f. klin. Chir., 1900, 62, 1, p. 14.
109. Guleke: Bruns Beitrage, 1908, V. 60, p. 673.
110. Lit. Burchardt Splanchnoptose in Ergebn. d. Chir., 1912, V. 4. Also Wiedhopf, Deutsche Zeitschrft. f. Chir., V. 128.
111. Rovsing: Die Unterleibs Chirurgie, F. C. W. Vogel, 1912.
113. See Borbjarg and Fischer: Arch. f. Verdauungskrankheiten, 1912, V. 18, No. 4.
114. Glenard: Les ptoses viscerales, Paris, 1899.
115. Fleiner: Munch. med. Wochenscht., 1895, No. 42-45.
116. Bial: Berlin. klin. Wochenscht., 1896, p. 1107.
117. Stiller: Grundzuge der asthenie, Enke, 1916.
118. Emma Schulz: Arch. f. klin. Med., 1914, V. 113, p. 402.
119. Wiedhopf: Deutsche Ztscht. f. Chir., V. 128.
120. Scarpa: Reale Stamperia Milano, 1809.
121. Moro: Brun's Beitrage, 1909, 63, p. 208-225.

## CHAPTER VII

### INTESTINES

The *length* of the small intestine varies considerably, with extremes of  $5\frac{1}{2}$  and 8 meters, and according to Dreike's measurements, a mean of about 6 meters (1). In childhood, according to the same author, the length of the small intestine is relatively greater than in adults; it is longer in men than in women, and in vegetarians than in those who eat meats; therefore, the small intestine, generally speaking, is longer in the poorer classes than in those more affluent. Beneke (2) states that for every 100 cm. of body length there are about 387.5 to 389 cm. of small intestine, and 91.5 cm. large intestine, but these figures do not hold for those races which are more purely vegetarian, as examinations of Japanese have shown.

The intestines are possessed of *great vitality*. In the experiments of Enderlen (3), loops were transplanted into the urinary bladder, etc. and Esau (4) who transplanted portions under the skin, found the coats intact microscopically even after separation of their entire mesentery.

*Intestinal secretion* is studied by means of so-called Thiery's, Vella's or Pawlow's fistulæ by which a section of the intestine is necessarily isolated (5). Even if the true physiological processes of secretion are not maintained ideally in such fistulæ, approximate knowledge of the mechanism and character of secretion is nevertheless gained. It must not be overlooked that what is investigated by such methods is not only secretion, but also absorption. The two cannot be separated. The net result is that the quantity which is actually secreted is not definitely known and this is especially unfortunate for comparison with pathological conditions.

In the *intestinal juice*, from both small and large intestine, a thin fluid secretion is differentiated from a semi-solid slimy material. The first carries the enzymes, one of which, the enterokinase, which activates trypsin, has already been met in discussing the pancreas. Another enzyme of the small intestines, the crepsin (6) does not split native albumen, with the exception of casein, but reduces the disintegration products of proteins, the albumoses and peptones, to crystalline substances. Among others may be mentioned arginase (found only in the mucosa and not in the secretions), nuclease, lipase, and various carbohydrate splitting enzymes. Of the latter, the lactase is particularly interesting, because, according to Weinland (7), it is present only during the suckling period, but may re-

appear in adult animals if they are fed regularly on milk sugar. Adolf Schmidt (8) believes that it is the absence of lactase in adults which is the cause of the diarrheas occasionally occurring in individuals who drink milk after having been unaccustomed to it for a long time. These individuals, however, easily reaccustom themselves to this diet. The purely diastatic enzymes of the intestines have only very weak powers.

Secretion takes place only when certain *stimuli of mechanical or chemical nature* reach the bowel wall. During starvation the intestinal mucosa produces no secretion; during hunger practically nothing flows from a Vella fistula, but secretion starts at once when a tube is placed in the opening, an observation not entirely without surgical interest (9). Of chemical substances, gastric juice, 0.5 per cent. hydrochloric acid, mustard oil, butyric acid, calomel, soaps and many others, stimulate secretion, but a very thin fluid, poor in enzymes, is poured out in response. To obtain a fluid rich in ferments and particularly rich in enterokinase, it is necessary that pancreatic secretion be present at the same time. Provision is thus made that the trypsin, inactive as it pours from the pancreas, is activated by the enterokinase which is secreted in abundance at the place where the splitting of proteins is designed to take place. There are also other examples which show the extraordinary purposefulness of the processes of intestinal secretion. If a woollen thread is placed in a fistula, a thin fluid is excreted; if peas or splinters of glass or similar objects are introduced, the fluid becomes much thicker. This, according to all investigations, obviously serves to envelop and glue together solid particles of food, and thus protect the mucosa (10). It is possible that the thick fluid also checks absorption, similar to the mucoid like factor in medicinal emulsions. That the secretion of intestinal juice is also dependent on the nerve supply is shown especially well in the so-called "paralytic" secretion. If all the nerves which lead to the loop in which a fistula has been made, are severed, an enormous secretion begins in a few hours, lasts for about 24 hours, and then is gradually abolished. During this paralytic secretion, the blood vessels are widely dilated and there is active peristalsis. It is usually assumed that inhibitory impulses are eliminated (11), but whether a hormonal as well as a nervous stimulus is concerned as in the pancreas, has not as yet been determined.

The *secretion of the large intestine* is not only less in quantity (a sixth to a seventh) but also less rich in enzymes, particularly in those which digest native proteins (in the small intestine there is trypsin and enterokinase). The fluid from fistulæ in the large intestine is therefore much less irritating to the skin. The thin portion is quickly absorbed, while the thick portion forms the chief part of the feces. *Feces*, indeed, are not as the layman believes, composed of only undigested residue; food remains

are really only a small fraction, and the chief bulk is formed of secretions or excretions of the intestinal canal plus bacteria. Thus in an isolated loop, closed at both ends, so much feces collect from secretion of the mucosa that rupture finally takes place (Hermann's fecal ring (12)). For this reason, a closed loop of bowel is never replaced in the abdomen if for any reason it cannot be resected; but is always sutured into the abdominal wall and a fistula established (13). A starving man also forms feces, as can be seen daily during certain after treatments in laparotomies. Fr. Muller (14) has estimated the amount of feces passed by professional fasters during a period of starvation; he found about 4 grams (3.818) to be the daily average. The moist feces weighed 22.01 grams. In an individual who is taking normal food, the amount is greater because all the glands along the intestinal canal, especially the liver and pancreas, are actively secreting; to this amount must also be added the residue of food which contains much insoluble material, for example, cellulose. But the actual amount of remnants depends not only on the kind and quantity of the ingested material, but also on individual peculiarities of the intestine itself. One normal individual may bring the same food material, especially cellulose, into solution, better than another (15). The old folk idea of "sensitive bowel" is thus confirmed by modern investigations.

Furthermore, the *quantity of intestinal contents* depends on the quantity of fluids ingested. If an artificial hyperæmia is produced by large infusions of saline solution (16), the intestines will accumulate a fluid feces-like material in such amounts that vomiting occasionally occurs. The intestinal wall will then become edematous.

*Absorption* from the bowel is not a simple physical process which can be explained solely by filtration or osmosis, but it depends on a "vital" activity of the intestinal epithelium. Writers are not agreed as to how far intrainestinal pressure influences absorption (17), but the experiments of Enderlen and Hotz (18) have shown that it is not increased, but decreased when stasis occurs in any portion of the bowel.

*Water* is very *quickly absorbed* in the uppermost portions of the small intestine and it is possible to make the stool fluid by saline infusions (15), only when large amounts are introduced.

The elective activity of the epithelium is shown even with salts; some are absorbed very easily and some with difficulty or only in minute quantities (19). Among food materials, the proteins are absorbed only after they are completely broken down to amino acids, or at most peptids, which, according to the present day conception, suggests that the body does not tolerate foreign proteins in its fluid. When a foreign protein in the food is broken down in the bowel, the body constructs from these building-stones a protein molecule which is specific for it, and which it



can utilize, and this synthesis of the specific protein molecule is probably begun in the intestinal wall, since thus far it has not been possible to demonstrate amino acids or peptids in the blood coming from the intestines (20) (see under Liver). Carbohydrates are usually absorbed only in the form of monosacharides, fats only when the various fat splitting enzymes and the bile have brought them into a soluble form. Fats, such as lecithin, which resist this solvent action are therefore not absorbed, but fat globules can readily be demonstrated just under the epithelium, a proof that the synthesis of fat, that is, the union of glycerin and fatty acids, has already been accomplished in this place.

The *absorption of the food* is practically completed in the *small intestine* (21), and according to Kaoru Omi (Rohmann), Frey (22) and others, more fluids and sugar are absorbed in the jejunum while the ileum absorbs more proteins and fats. It is only in over-nutrition or in catarrhal conditions which injure the mucosa, that a noteworthy amount of food will pass through and enter the colon. This applies, of course, only to food free of detritus, not to food rich in cellulose. The latter is hardly touched in the small intestine and is split only by the bacteria in the colon. With this knowledge, a patient in whom it is necessary to establish a fistula of the small intestine will be given food as free as possible from detritus. Chopped meat is the best, so that in spite of the fistula he will obtain sufficient nourishment without being troubled with excess leakage. The much favored barley soup is less useful because, according to Heile's investigations, it forms large amounts of feces.

In comparison to that of the small intestine, the *absorptive power of the large intestine* is very small. Unchanged protein is not absorbed at all. About 20 per cent. of the sugar is taken up and certain amounts of split proteins. Water is absorbed in about half its amount, and this fact is useful clinically when patients, who cannot drink after operation, are given the necessary water by the drop method. Since alcohol is also well absorbed, wine and sugar are added to the fluid. Furthermore, the colon seems to be of importance in the absorption of alkali, but we are not particularly well informed of this fact, especially concerning its pathological physiological importance.

The *motive power of the intestinal movements* lies in the musculature, of which there is a longitudinal and a circular layer. Ganglion cells are embedded in the former. In the colon, the longitudinal muscle, which is arranged tape-like, is differentiated from the circular muscle which surrounds the bowel with one continuous layer. Roith (23) assumes that the amount of circular muscle becomes greater as the anal end is approached but Rost's planimetric measurements have disproved this idea (24). The longitudinal layer is arranged tape-like to the sigmoid

flexure, and cannot be compared functionally to that of the ileum without reservation, since it is, according to Rost, in almost the same state of contraction as the circular musculature. The tapes act functionally like elastic bands and by their tension keep the bowel shortened and cause the formation of those depressions formed between the plicæ semilunares.

The following methods have been used to observe the movements of the intestines under physiological conditions. First, observation on an excised organ or after laparotomy, when it is necessary to cover the intestines with Ringer's or Tyrode's solution to preserve the approximate physiological conditions; second, by means of the x-ray, and third, by means of an insert of a transparent celluloid window in the abdominal wall, according to the technic of Katsch and Borchers (25). Each of these methods has its justification, each has its advantage and disadvantage, none is absolutely superior to the other.

If we study first the *movements of the small intestine*, exclusive of those of the muscularis mucosæ, we differentiate a "mixing movement" and a so-called peristaltic wave, the latter of which drives the chyme forward. The *mixing movements* which arise from rhythmic contractions of the intestinal muscles are of two kinds: kneading, from simultaneous contraction and relaxation of the longitudinal and circular muscles (Cannon), and pendulum movements from alternate contraction and relaxation of the muscle layers of segments of bowel of varying lengths (Starling, Magnus (26)). Whether these mixing movements serve as their name implies, only to mix the chyme, or whether, as Rieder emphasizes, they are of great importance in food absorption by influencing the local blood and lymph circulation, has not been decided. Still another form of movement has been called Exner's needle reflex. This consists of contractions and relaxations of the muscularis mucosæ when the mucosa is irritated by a sharp object such as a needle or a splinter of bone. It bulges out and attempts to force the pointed end downwards. In its purpose, this movement is typical of the general movements and reflexes of all smooth muscle. Thus pins, etc., which have been swallowed point downward, are turned in the bowel and pass onward, head first. This "marginal current," as it is also called, can be directed either toward the anus or toward the stomach, and is independent of the direction of movement of the centrally placed intestinal contents, which, of course, are always directed toward the anus. It is demonstrable in the stomach as well as in the small and large intestines. If corpuscular elements are introduced in an enema, the small particles can be carried far upward by this marginal stream, so that Grutzner (27) who made these investigations, found lycopodium granules which had been injected in an enema, in the stomach. But these findings,

by no means prove a true anti-peristalsis of the bowel contents. In fact, it is possible that the reversed direction of the marginal current in Grutzner's experiments, was due to the sodium in the sodium chloride solution, for Nothnagel (28), had observed that the other muscle layers of the intestines also showed an ascending wave of contraction if he touched the intestine with a sodium salt. Grutzner especially emphasizes that he could demonstrate the lycopodium in the colon and ileum only if it was suspended in saline solution; if he used water the granules remained in the rectum.

The *peristaltic wave* serves to move the bowel contents forward and consists of contraction of one segment and relaxation of the next segment toward the anus. Like the mixing movements these peristaltic waves are stimulated by distention of the bowel; an empty loop lies quiet and motionless. But progressive movement begins only when a certain internal tension is reached and is not merely proportional to the state of filling of the intestine. This was shown by Trendelenburg (29) who used the intestines of guinea pigs, which are particularly well adapted to such experiments because the mixing movements and the changes in tonus are absent. This principle of filling the bowel is, of course, often used therapeutically to produce a quicker emptying, for example, when a saline cathartic is given, its osmotic pressure prevents the absorption of fluid from the stomach and upper intestines, and therefore provides the necessary filling of the bowel to stimulate peristalsis, and a quicker emptying of the small intestines results. Furthermore, the "peristaltic effect" also depends, according to Trendelenburg, on the rapidity with which the bowel is filled; a fact which explains the well known laxative effect of a glass of water, which is taken in the morning on an empty stomach. If the filling takes place too slowly, peristalsis frequently does not occur at all, but this approaches the pathological. Later, in discussing peritonitis, it will be seen that the so-called intestinal paralysis is simply a result of distention and not its cause. This overdistention must, therefore, be guarded against in giving saline cathartics in cases of chronic ileus or similar diseases.

This "classical" form of peristalsis in which the feces are moved forward step by step, is, according to the general opinion, the usual way in which the intestinal contents are transported. There is, however, another movement—the so-called "rolling movement" or peristaltic rush, in which the contents are forced very quickly through longer stretches. Some authors believe that this is nothing but an increase of normal peristalsis, but this has not been proved. It seems easier to believe that in this type of movement a sort of "squirting mechanism" is involved, and Albert Muller's (30) well-known experiments give substantial support

to this idea. With Hesky and Kondo, he showed that dogs, in which large areas of longitudinal and circular musculature of the small and large intestine were removed, still had normal fecal evacuation. Removal of the longitudinal musculature alone led to a certain resistance in the denuded area, but not to absolute obstruction. This fact can be explained in but one way, *viz.*, that the segment of intestine above the part devoid of muscle is capable of squirting its contents through the immovable portion. David's (31) *x*-ray studies in which he showed that the masses of bismuth slide forward rather rapidly in a tape like manner also seem to favor such a theory.

The much discussed question of "*anti-peristalsis*" assumes a new meaning if regarded from this viewpoint. But the anti-peristalsis of the small intestine and that of the large intestine must be differentiated. In very elaborate investigations, consisting of resections, reversal and reuniting of loops of small intestine, a number of workers attempted to solve the problem of the actual existence of anti-peristalsis (32). Some of the investigators reversed the small intestine throughout almost its entire length and found that not only was defecation regular but their animals remained in nitrogen equilibrium; therefore, Muhsam, Enderlen and Hess concluded that an anti-peristalsis was actually one of the movements of the small bowel. Curiously enough, this conclusion was completely rejected by Putz and Ellinger on the basis of investigations quite similar in principle to those of the former. From the presence of a large amount of indican in the urine, from the dilatation of the bowel above the reversed loops, and particularly from observations of the intestines in a saline bath after the injection of pilocarpine, these authors concluded that a reversed movement did not take place. But the fact remains that feces are moved forward through the reversed loops and in conjunction with Muller's findings, that defecation is normal in a dog, even after complete removal of its bowel muscle, it really seems probable that peristaltic waves are not the exclusive agents which move the feces, as has always been assumed. Perhaps, as stated above, a squirting mechanism is very important after all. Further investigations of this question are very necessary, particularly *x*-ray examinations, to show how chyme passes through reversed loops.

It is due to a combination of these different movements that portions of small intestines always resume their proper place in the abdominal cavity, no matter where they are put. This fact, observed often enough at operation, has been studied with the *x*-ray by Bose and Heyrovsky (33) who marked the part in question by suturing birdshot or similar objects in its wall. Observations through windows in the abdominal wall have shown that the position of the intestines varies with the kind of food consumed (Plenge, personal statement).



The *colon*, also, is not usually at rest, as is often assumed, but is always moving, though slowly. The x-ray examinations of Schwarz (25) show that there are two pronounced kneading movements, a bulging out and a pulling in of the wall, and displacement of the loop first toward the anus and then toward the stomach, usually around a fixed point. These alternate with the so-called large pendulum movements designated by Raiser (34) as "waving" movements. These "mixing and kneading movements" are seen principally in the proximal colon where the feces first come to a stop; but they also occur in other segments.

The second group of movements described move the contents forward. These must be differentiated into two forms; first, slow peristaltic contractions, and second, the so-called great colon movements; both occur, doubtless, coincidentally in the same individual. A controversy exists only as to whether certain of the movements should be regarded as the beginning movements of defecation, but this question is of little practical importance. This great colon movement, indeed, is the first which has been observed in man with the x-ray. Holz knecht (25) saw, in a patient with presumably normal bowel, that a bismuth meal, which had filled the left flexure, was pushed from the transverse into the descending colon; within a few seconds, the constrictions of the transverse colon disappeared and rest then supervened. The patient had no perception of this colonic movement. Holz knecht later made a similar observation; since then, such great colon movements have not been seen, but by serial pictures taken at half-hour intervals, it can be satisfactorily shown that such movements must have taken place between two exposures. Therefore, it is proved, that in normal individuals, independent of defecation, the feces are forced forward by this particular form of movement, for a considerable distance in the colon, in a few seconds of time (25). According to Bayliss and Starling (35) the same laws, which apply to the small intestine, also apply to the small "regular peristaltic movements" which can be seen through the fluoroscope in the descending colon (Rieder (25)). By stimulation from within, contraction in this segment occurs with dilatation in the loop just beyond, and thus the fecal masses are forced forward. This is easily demonstrated in the large intestine of the rabbit, whose feces form in small hard balls, which fill the distal part of the colon, like a string of beads, and each ball is pushed forward individually (Langley and Magnus (25)). In man, this form of movement, under normal conditions, progresses very slowly (serial pictures of Rieder).

But in addition to the movements just described there are others which propel the feces backward from the anus. As has been explained above, a true anti-peristalsis over long stretches cannot be obtained experimentally by reversing loops of small intestine, but it does occur in the colon par-

ticularly in the proximal part. Cannon was the first to show these waves by  $x$ -rays of cats, and his findings have been amplified and confirmed in all essential points by Elliot and Smith. In man, this anti-peristalsis has also been shown conclusively by Stierlin, Bloch, Bohm, Rieder (36) and many others. With serial pictures, Rieder could see first an anti-peristalsis which rapidly extended over the whole colon from the rectum to the cecum, and second, small anti-peristaltic movements confined to the proximal colon.

These intestinal movements are dependent on the *nervous supply* of these structures. Exactly as in the heart, there is, first, an independent nervous apparatus in the intestinal wall (longitudinal muscular layer) in the form of Auerbach's and Meissner's plexus, and second, an extrinsic supply through the sympathetic and the cranial or sacral autonomic system. The pendulum movements, as well as the peristaltic and anti-peristaltic activity are dependent on the presence of Auerbach's plexus (Elliot and Smith (25)), so that this peripheral nervous system must be considered the actual motor center which is controlled by stimulating and inhibitory fibres from the long nerve tracts. Stimulating impulses come not only through the cranial autonomic or the sacral system but also from the vagus or from cerebrospinal fibres from the lumbar and sacral segments (N. pelvici et erigens). Inhibitory fibres which reach the intestines by way of the sympathetic arise in the celiac ganglion, in the superior and inferior mesenteric plexus, that is, directly through the splanchnics. Stimulation of the sympathetic leads, therefore, to a slowing of the movements or a relaxation of the intestines. The results of experiments on vagus stimulation, however, are not in entire agreement, chiefly because of technical reasons (see Bohm (37)), but stimulation of the autonomic fibres always results in tonic contractions. The experiments on the large intestine have a particular interest because they show that stimulation of the vagus leads to a tonic contraction of the proximal colon (Bohm), while stimulation of the lumbo-sacral plexus produces a contraction of the distal colon (Bayliss and Starling, and Elliot and Smith), that is, the large intestine is not a functional unit, which fact makes its physiological movements and the disturbances in these movements very much more comprehensible. To emphasize this functional difference, the large intestine is now divided into a proximal, intermediate, and distal part, thus abandoning the old anatomical divisions (Elliott and Smith).

*Bauhin's valve*, under normal conditions, prevents backflow from the colon into the ileum. Its action depends first on a ventilator-like arrangement of the valve leaflets, and second, on a contraction of the annular muscle surrounding the valve, the so-called ileo-colic muscle. This sphincter is said to be closed when at rest (Elliott, (38)), and it contracts

firmly when the splanchnic is stimulated and opens on stimulation of the vagus, according to Katz and Winkler (39). Section of the splanchnic or destruction of the spinal cord leads to a relaxation of the tonus of the sphincter. The valve is not competent in the new born and in sucklings, and an insufficiency in adults is seen not rarely, especially after enemas. Dietlen with the  $\alpha$ -ray could find in about every fifth case, a re-entrance of bismuth from the cecum into the ileum (40). It seems that in these cases of valvular insufficiency there is usually some chronic disease of the cecum or its immediate vicinity. Since, however, as stated above, Grutzner found lycopodium granules high up in the small bowel and in the stomach, after enemas, in entirely normal animals, it is necessary to be cautious in the diagnosis of an insufficiency of Bauhin's valve as recognized with the  $\alpha$ -ray. Then, too, it is possible that certain substances of special chemical nature may have an influence on the opening and closing of the normal valve from within the cecum. In general, however, the valve prevents a back flow from the large intestines, and also remains closed when the pressure there is fairly high, as for example, in large intestinal ileus. A ballooning of the small intestines is found but seldom in cases of marked distention of the cecum. Indeed, according to the experiments of Heile (21) it seems that the filling of the colon causes a firmer contraction of the sphincter in a way analogous to that of the pylorus, for in experiments performed for a quite different purpose, he showed that the introduction of a tampon cannula into the colon produced a much slower evacuation of the contents of the small bowel through an appendix fistula. This is due to an increased contraction of the ileo-colic muscle following the mechanical irritation produced by filling the colon. A sudden massive filling, such as occurs with the enemas employed by von Genersich and Dauriac (41) (from six to nine litres under 100 c.c. water pressure) is necessary to spring the valve.

This valve is interesting from still another viewpoint; as is well known, this is the favorite region for invaginations; indeed, an "ileo-cæcal invagination" is quite commonly found. But Blauel (42) could show that the valve itself is not at fault, but that it is more probably due to a bulging of the wall of the cecum, and the valve is pulled along with it (see under ileus).

From investigations of Luschka, Henle and O. Krauss (43), it was always thought that the layers of muscle in the small intestine divide at the junction of the ileum and cecum in such a manner that only the ring muscle enters the valve and the longitudinal layer spreads out on the surface of the large intestine. Such an arrangement of the muscles would, of course, favor the development of an invagination in this region. Toldt (44), however, demonstrated that a number of the longitudinal

fibres also enter the valve and mingle with the circular fibres; with this arrangement an invagination of the valve is anatomically almost impossible.

Before we leave this subject, the physiology of *defecation* and the actual evacuation of the feces must be briefly discussed. During this process, there is a series of movements of the intestines, abdominal walls and pelvic floor, all dovetailing one into the other, so that an evaluation of the separate movements is extremely difficult. There is no doubt concerning the importance of the pressure of the muscles of the abdominal wall. A personal trial is convincing enough. The movements of the large intestine shortly before and during defecation are much less understood. Schwarz (25) investigated this subject, by stimulating defecation artificially, with soap enemas after a bismuth meal. In agreement with similar but less normal experiments of von Bergmann and Lenz (45) he found first, a "rocking movement," which mixed the enema and the feces, liquefying the latter, and second, the large colon movements already mentioned above, that is, those energetic contractions of the transverse colon which move its contents forward. Both of these forms may be considered the prelude to actual defecation. There then follows the important movements of the distal colon, especially those of the sigmoid flexure, which occur only when a certain degree of filling exists; in the interim, the sigmoid is motionless. This is of especial interest to the surgeon, because the periodic activity of the distal portion of the colon explains why patients even after complete destruction of the sphincters, evacuate feces at intervals and not continuously. The rule was given by O. Beiru that the feces collect in the sigmoid before defecation, and do not enter the rectum. This has been disputed many times, but was recently verified by Strauss (46). In fact, the rectal ampulla is normally empty of feces and the passage of feces from the ampulla to the rectum is followed by the sensation of a need for defecation. Of course, normally, the stool can still be controlled by the sphincters. That many people, especially bedfast children, often have the rectum packed with feces, does not disprove the rule; this enters the domain of pathology. It will be shown, when constipation is discussed, that the sensitivity of the rectum is of quite especial importance for regular defecation. If this is completely destroyed, as in fractures of the spinal column, it may lead to a very grave retention of feces in spite of the relaxed sphincters, and evacuation will only take place at haphazard times when the rectum is filled almost to the point of rupture. The actual motive power for defecation is supplied by the pressure of the abdominal walls and intestinal movements, and both are activated reflexly by the desire to defecate, which, in its turn, is a result of stimulation of the rectal mucosa.



The *innervation of the distal end of the large intestine* is through the sacral-autonomic system, that is, from branches of the lumbar and sacral nerves. But there are fibres from the inferior mesenteric and the hypogastric plexuses in addition. Those of the latter supply the mucosa of the anus and rectum with sensory and motor fibres (von Frankl Hochwart-Frohlich (47)). The sphincters act as a regulating inhibitory mechanism.

The internal sphincter, containing smooth muscle, should be differentiated from the external sphincter, which consists of striped muscle. The latter is assisted by the levator ani and acts in many ways like an involuntary muscle. It does not degenerate, for instance, after section of its nerves (Goltz and Ewald, etc. (48)). The sphincters normally close "independent of the will but dependent on the nervous system" (tonus, in the sense of Heidenhain, von Frankl Hochwart). Indeed, the internal sphincter can develop considerable tonus, so that operative injury of the external sphincter alone does not usually lead to incontinence as, for example, in deep incision of an anal fissure (Boyer). Nevertheless, the two sphincters are very closely related in man (49), so that the animal experiments (von Frankl Hochwart and Frohlich) in which it was found that they were completely independent, cannot be applied without reservations.

The activity of the anal sphincters is directed from varied centers. In the first place, each contains its own center, which consists of ganglion cells located in the musculature. This fact, showing a certain analogy to cardiac muscle, is peculiar to the external sphincter which consists of striated muscle (50). These ganglion cells gradually bring about a tonus of the sphincters even after complete destruction of the spinal cord and the sympathetic fibres, and the incontinence which occurs at first is replaced by a condition which is much more bearable. Even if these patients are not aware of the act of defecation on account of the destruction of sensory fibres, the feces, as long as there is no diarrhea, are evacuated at intervals, and not continuously (51). This local center is governed by a second center situated in the sympathetic ganglion (inferior mesenteric). There are also centers in the *conus terminalis*, in the lumbar region of the spinal cord, and one in the cortex, but the position of the latter varies in different species of animals (52). The importance of these defecation centers should not be underestimated, for even if the sphincter tonus is preserved in some animals, when the spinal cord is totally destroyed, along with the inferior mesenteric ganglion (von Frankl-Hochwart and Frohlich), Roussi and Rossi (53) and others could show plainly perceptible disturbances, *viz.*, partial incontinence and relaxed sphincters, in dogs and monkeys even five months after the destruction

of the conus terminalis. The same is observed in patients with injuries of the spinal cord, as, for example, after fractures of the vertebræ. In addition, an open anus is found when movements of the colon are absent and after interruption of the sensory paths, that is, after section of the posterior roots of the sacral spinal cord (54).

By diarrhea is understood a massive evacuation of fluid feces (55). Our knowledge of the form of movements of the various portions of the intestines in diarrheas is very meager and depends on indirect conclusions. For example, it is not at all certain that they are similar to those movements which occur during *catharsis*. Observations of the latter condition must be used for analogy and may now be discussed. The *x*-ray examinations of Stierlin and Meyer-Betz and Gebhardt (56) have shown that senna electively increases the movements of the large intestine so that the feces hurry through it in from one to two hours. Aloes increases the tonus of the musculature of the large intestine, so that this drug gives rise to symptoms similar to those of spastic obstipation. Castor oil leads to an increase of fluid contents, even in the small intestine; and larger masses of fluid, therefore, reach the large intestine. As a result of the stretching, there are sudden large movements of the colon, and a fluid stool is evacuated. Feces remain in the colon after castor oil about as long as after senna, but since the senna stool is mushy and the castor oil stool is fluid, it appears that castor oil also inhibits the absorption of water in the large intestine. Gas bubbles can be seen by the *x*-ray and with castor oil, may fill the entire large intestine. They stretch the walls and incite large colon movements. Probably they are an expression of this defective absorption. Jalap and the saline cathartics lead to increased secretion in the small intestine. At the same time jalap stimulates the mucosa of the colon, while the final defecation after saline cathartics is similar to that after castor oil. If the latter is given with the intestines filled, the fluid and the gas push past the older fecal contents and take but little of it along. The bowel is thus not emptied at all. Calomel is the substance which stimulates both small and large intestine, without leading to increased secretion, and all of the contents are pushed forward.

If we apply the findings in catharsis to the *pathological diarrheas* we must doubtless assume that there is increased activity of the colon, which may be of two forms—either an even increase in movements or, so to speak, movements in answer to the increased filling from slow absorption, the combination taking the form of an explosive evacuation after a few large colon movements. As a superimposed reason for this accelerated emptying of the colon, it must be assumed, as with senna, that there is a stimulus to the motor fibres controlling the colon movements, or an indirect stimulus from delayed absorption and increased secretion which produce a too great and too sudden filling.

What can be the cause of this stimulation of the motor apparatus? The simplest conditions probably occur in the ordinary acute diarrheas which may appear after a dietetic error. There results one or two semi-fluid evacuations, followed by a certain amount of sensitiveness of the bowel for another day. Then all disturbances cease. The stimulus in this case is undoubtedly the unsuitable food, but it is not because it should be expelled as quickly as possible that there is diarrhea, but because the food initiates a purely reflex stimulation. The whole affair can perhaps be quite well compared to the appearance of an urticaria occasionally following the consumption of certain fish. If there is a transudation of fluid into the subcutaneous tissues in urticaria, there may also be a similar leak into the intestines in these reflex diarrheas (perspiration of the bowel) (57). That this increased secretion is actually the cause of the diarrhea has been shown by numerous examinations and weighings of the feces; and according to the present idea, it takes place in the colon at a time when the offending food is still in the small intestine. Delayed absorption in the small intestine can hardly play a role in the fluid condition of the stool since even in severe diarrhea, it is rarely possible to find in the feces, sugar or other substances, which are easily absorbed (Strassburger). The diarrheal stool is also quite different, even grossly, from the material passed through a fistula of the small intestine. An increased peristalsis, therefore, is not the only cause. It is only in the very rare jejunal diarrheas that a stool having the properties of the contents of the small intestine is evacuated. In this case, there must be an accelerated peristalsis in this part of the bowel.

It is a fact, well known also to the layman, that certain individuals react to various foods with almost certain diarrhea. Furthermore, some in the same condition of nutrition, develop diarrhea very readily, and others never. A "bowel weakness" is spoken of quite generally, but an effort has been made, particularly in the chronic cases, to establish groups. Thus, as A. D. Schmidt and Strassburger (58) first pointed out, there are patients who develop diarrhea upon consuming any kind of carbohydrates, probably because, according to the present idea, their intestines cannot split carbohydrates, especially cellulose. The contents, assisted by bacteria, therefore, ferment in the large intestine (fermentation dyspepsia). The more or less fluid feces, and especially the gas, lead to accelerated peristalsis and to a secondary increase in the secretion of the colon. Primarily, however, there is constitutional weakness of the ileum, since we have seen above, the splitting of carbohydrates takes place here.

In another group of cases, carbohydrate digestion is normal, but the digestion of muscle and connective tissue is disturbed. This last form is often due to achylia of the stomach (59). In the absence of pepsin and

hydrochloric acid, the connective tissue in meat is not dissolved and only roughly comminuted fragments enter the intestine and there decay from bacterial activity. These decomposing masses irritate the bowel and lead to diarrhea. Intestinal bacteria, therefore, only play an intermediary part in this process. It is not a question of the development of certain kinds of bacteria, or even an increased virulence of those present, but only a purely quantitative increase in number, due to favorable conditions of growth.

Disturbances of absorption in the small intestine may also lead to the development of diarrhea, especially when the absorption of fat is hindered in the presence of tuberculous mesenteric lymph nodes (*tabes mesenterica* or tuberculous peritonitis). The absence of pancreatic secretion will also lead to fatty stools and to symptoms of defective fat absorption. Quite peculiar is the hypersensitiveness of some patients to even a small quantity of hen's egg albumen. Schittenhelm and Weichardt (60) believe that the intestinal wall of such patients is permeable to unchanged egg albumen. As always, when foreign protein is introduced into the blood stream, a hypersensitivity to this particular protein develops, and the ingestion of even the most minute quantity will lead to a kind of anaphylactic shock, expressed in these cases by diarrhea. It has been thought that the diarrheas in non-ulcerative tuberculosis, in exophthalmic goiter, etc. might also be explained in this manner, but the ideas are only unproved hypotheses.

Intestinal movements are also dependent to a great extent on the nervous system, even in healthy individuals. Diarrheas, from fear or excitement or other psychic factors are quite common. Here also the question is not of accelerated peristalsis, but of an increased secretion into the bowel.

Thus far, we have discussed only the disturbances of intestinal functions which show no anatomical changes. If the latter are present, we speak of an *intestinal catarrh*, an *enteritis*, or a *colitis*. Intestinal dyspepsias form a basis for understanding the functional disturbances observed in inflammatory processes. The differential diagnosis is founded on the abundant excretion of inflammatory products (mucous, pus, blood). In the etiology, especially of the acute varieties, bacteria (typhoid, paratyphoid, and streptococci) play a large part. Furthermore poisons, organic and inorganic, whether they enter through the mouth or from the blood, are also important exciting causes. Both routes are often combined. Mercury poisoning, for example, leads to "an excretion inflammation" in the colon; in addition there is occasionally a corrosive action in the stomach (61). It is an open question in mercury poisoning whether its action is due to the excreted metal or is a result of thrombosis and other



injuries to the vessels. Many other poisons are also excreted into the bowel and may cause severe inflammation of the mucosa in the process. The same explanation is given for the enteritis in nephritis, in severe burns of the skin, and in general sepsis. How much of a part anaphylactic phenomena play in the inflammations following poisons of a protein nature (see above), has not been sufficiently investigated.

In the *bacteriological etiology of acute enteritis*, the question of non-specific organisms, especially colon bacilli, is very important. The occasional demonstration of *B. coli* in the blood, proves that this usually saprophytic organism can become pathogenic under certain changed life conditions. Whether the advent of a pathogenic colon bacillus is necessary or whether an organism within the bowel may suddenly acquire virulence is still an open question. Both possibilities are reasonable.

The cause of such a severe enteritis is often not recognizable. This is especially true of the colitis which is occasionally observed after operation (62). Anschutz (63) has observed them particularly after operations on the stomach and believes that they are produced by poorly digested food masses entering the intestines which have become hypersensitive through fasting, etc. Riedel thinks of mechanical injuries (pressure from intestinal contents). Muller (64) denies that they are true dysenteries. According to our experiences, these explanations are not sufficient. Patients whose intestinal tract was entirely normal, have often been the victims of this very grave post-operative acute colitis and at autopsy a destruction of the entire mucosa of the large intestine is found. We saw this, for instance, in a child, after Forster's operation, and the impression was gained that it was actually due to a chemical poison; but in the cases known to me, no such poison could be found, nor did the kidneys show, for example, the characteristic changes of mercury intoxication.

In *chronic inflammation*, the ordinary chronic infectious organisms such as *B. tuberculosis*, *actinomyces*, *spirochæta pallida*, play a part in only a few of the cases. The etiology of the majority, especially those suitable for surgical treatment, such as the interesting forms of ulcerative colitis, is entirely unknown. A good result is occasionally achieved by short-circuiting the feces through a fistula or an artificial anus and treating the bowel from above by irrigation. The success resulting from such treatment seems to show that the feces are a continuous source of irritation to the ulcerated area. An ulcer once formed, becomes chronic, probably because of the poor local conditions for healing, but whether other etiological factors co-operate, cannot be answered in a way applicable to all cases. Sometimes there is a constitutional disease which produces a lowered tendency to heal (gout, leukemia and scurvy and others). In other cases, a constitutional intestinal weakness, such as has been

described in dyspepsias, may possibly be operative, but very frequently the whole process is one of poor healing of an acute inflammation. For instance, cases of gonorrheal proctitis which appear very hopeless and have persisted for years, often heal rapidly after the establishment of a fistula.

Those cases of enteritis often associated with extensive *ulceration* do not, however, always show diarrhea—the latter is often absent when the ulcers are present in the lower small intestine and in the cecum, while it is present more frequently in ulceration of the lower colon. Whether diarrhea is present or not in ulcerative processes, depends, according to A. Schmidt, on the condition of the mucosa between the ulcers. To produce diarrhea, it is necessary to have secretion, and this is absent in the ulcerated areas. For this reason, a classification of enteritis cannot simply be made from the slightest to the most severe, and including finally, those with ulceration. Even if such a grouping is justifiable in isolated cases, some pathological physiological peculiarity must nevertheless be present when ulcers appear.

Irritating conditions within or about the rectum lead to *tenesmus*. The explanation of this condition is clear from the statements regarding the physiology of defecation.

Delayed evacuation of the bowels, that is *chronic constipation*, has only recently awakened surgical interest since attempts to eliminate or improve this disturbance have been made.

Although, theoretically, constipation may have its origin in any part of the gastrointestinal tract,  $x$ -ray investigations have shown that the usual reason is disease of the motor apparatus of the large intestine. Since the colon is structurally not a unit so far as its innervation and movements are concerned, it furthermore appears advisable to recognize a classification, according to the locality where the stagnation of the feces occurs. This can be done by means of the  $x$ -ray. It is more important, however, to observe when the shadow of the bismuth appears in a certain segment of the intestine than the length of time that it remains visible in a higher segment (65).

The *most frequent form of constipation is the proctogenic* (66). This has been known relatively for the longest time since the diagnosis is comparatively simple, that is, can be established by the introduction of the finger. About 60 per cent. of all cases fall in this group (67). Among the causative factors of this form, are, first, mechanical obstructions in the rectum or in the neighboring parts of the bowel. In the case of tumors within or without the colon, congenital or gonorrheal strictures, loops of the descending colon (68), the constipation is only a symptom of an entirely different disease. No difficulty in the explanation of the pathological physiological

processes, is presented in these cases, although frequently a rectal carcinoma is treated as simple constipation until it is too late for operation. This form of obstruction should be classed with ileus, just as the obstruction in Hirschsprung's disease (69), or the kinking of the sigmoid flexure against the rectum which is pathologically physiologically related to Hirschsprung's disease (70). Far more difficult to evaluate, in relation to constipation, are the hypertrophic folds of Houston, that is, the folds at the junction of the anus and the rectum which represent the remains of the anal membrane (71). Gobel (72) destroyed these folds by means of special crushing forceps and obtained good results in this type of constipation. They are much discussed as causes of constipation, in English and American literature.

Secondly, the proctogenic type of constipation is found in increased tonus, that is, spasm of the sphincter. The primary relation of both disturbances is also shown here by the good results from appropriate therapeutics. If the spasm of the sphincter is abolished by dilatation, the constipation is cured, often permanently (73). That the cause of these spasms is usually a painful affection in the region of the anus, especially fissures, is probably true from therapeutic results in numbers of cases, but the failures show that it is not always such a simple disease. Patients with fissure ani, complain chiefly of pain at the moment of evacuation of the stool. The fissure is exceedingly painful on rectal examination and the sphincter is spasmodically closed. But other patients complain of severe pain, also, which begins one to two hours after defecation, but is different in type from the local pain at the point of the fissure, although its starting point is usually in the sphincter. These after pains sometimes persist, even after the fissure should long have been healed by incision or stretching, and when the pain, during the actual evacuation of the stool is entirely absent. It can hardly be doubted that it bears a certain relation to the fissure, since intelligent patients state positively that it began with the fissure. To speak of a reflex, is nothing more than to avoid the issue and whether there is an analogy to lead colic—atropin usually has no effect whatever—is thus far completely unknown. The most probable explanation is that there is a more extended spasm of the colon, which is possibly responsible for the constipation, also. Locally there is found, according to the microscopical examinations of Quenu and Hartmann (74), a neuritis of the terminals of sensory fibres, and while the reflex spasm of the sphincter is sufficiently accounted for by this finding, it fails to explain the after pains.

The tonus of the sphincter varies very considerably in different individuals. Rossolimo (75) made extensive investigations of this subject, and found that it is increased in neurasthenics among others,

and also in certain nervous diseases, particularly those affecting sensory paths, the whole having been summed up as rectal neuralgia (76). In all such cases, a constipation of proctogenic type may result from this increased tonus.

A third finding often seen in proctogenic constipation and which doubtless has an etiological relation to it, is a lowered sensitivity and motility of the distal end of the intestine. Although corresponding anatomical findings have thus far not been found, there is a certain amount of experimental and clinical data concerning severe lesions of the nerves, which helps to explain some of the lesser disturbances which we meet in this condition. Thus it has been shown experimentally, that after section of the posterior roots of the sacral spinal cord no movements of defecation can be incited through sensory stimuli (54). Furthermore, constipation results from destruction of the lumbar segment of the spinal cord (Goltz), either experimentally or from pathological causes (tabes (77)). Since there is, of course, interruption of the reflex arc in all these cases, it is clinically, very often difficult to decide whether the injury is to the motor or to the sensory mechanism. In many cases, not depending on severe nervous diseases, there is often a proof of the described disturbance in the innervation of the distal end of the intestine by a failure of the reflex movement of this portion on the introduction of a proctoscope or after distension with air. This is also often encountered in high rectal carcinoma. Here the palpating finger finds a wide, relaxed ampulla, and this is actually a suspicious diagnostic sign if the tumor is located too high to be reached by the finger.

Finally, among the causes of proctogenic constipation, disturbances of the accessory muscles of defecation (diaphragm, levator ani, abdominal walls), may be mentioned. Practically, it is often very difficult, in a given case, to decide how much is due to this poorly functioning accessory apparatus, since weakness of the muscles is only a sign of a general muscular weakness; *i.e.*, an asthenia, in the sense of Glenard and Stiller (78). Pinkus (79) describes a special form of constipation belonging in this group. He calls it "*constipatio muscularis sive traumatica mulierie chronica*," a constipation due to a weakness of the pelvic diaphragm following the trauma of childbirth. The statement regarding asthenia covers this type. But how small a part weak abdominal muscles actually play in regular bowel movements is shown by a case of Hertz (65), who observed a child with complete congenital absence of the entire abdominal musculature which, nevertheless, had very regular stools. That hernia may also occasionally cause constipation is shown by a case of Ebstein (80) in which an appropriate operation completely cured the constipation. In general, however, hernias have nothing to do with



proctogenic constipation, and similarly, the numerous sections of the phrenic nerves, according to the method of Sturtz and Sauerbruch (81) have shown that the diaphragm is not as important in defecation as has been assumed.

Although the designation "proctogenic constipation" covers a variety of conditions, nevertheless, the disease pictures correspond insofar that in each case the distal end of the bowel is the seat of the obstruction. This is unquestionably of importance in treatment, and this classification therefore should be retained for the present.

An attempt has furthermore been made to contrast an "*ascending type*" with the proctogenic type (82). This grouping, however, gathers very different etiological forms into a seeming unity. Fecal obstruction in the proximal colon does not occur only in "weakness" of the cecum in its broadest sense, but also when the seat of constipation is in a deeper segment of the bowel (73). In this way, the name may be misleading, but it is widely used, and has led to resections of the cecum in those more severe forms of constipation in which, by the x-ray, the intestinal contents were demonstrable abnormally long in that portion of the bowel. If the actual seat of trouble in such cases was below the cecum; if, for instance, it was proctogenic, where the fecal stasis in the cecum was secondary, the resection naturally did not give relief (73).

The experiments of Bohm (83) have, of course, shown that constipation confined solely to the proximal end of the colon is conceivable and may be explained as a consequence of vagus stimulation. He found, indeed, in cats, and even better in rabbits, that after vagus stimulation, there was increased anti-peristalsis and mixing movements in the proximal colon, with tonic contractions at the end of the same structure. We cannot say with certainty at the present time, in the absence of anatomical findings, that such a form of constipation occurs in man. Some x-ray pictures seem to speak in its favor (84). But then it would be necessary to accept the theory of a constipation due to irritability of the large intestine and return again to the "spastic constipation" of Fleiner, which has been completely refuted (85).

Other x-ray findings have, however, taught us the justification of Fleiner's idea that a constipation caused by increased irritability of the colon can occur. The tonus of the colon, as shown, for example, by enemas, is indeed very varied. Singer and Holzknecht, Schwarz (86), Stierlin, and others, have published x-ray reports showing that there may be a diminution in the size, indeed, a tape-like pulling together of the entire intermediate and distal colon, beginning with the transverse portion. A "hyperkinesis" of the proximal colon was also found in such cases, a proof, as far as we may judge at present, that the different forms of

"spastic" constipation, or if preferable, the "constipation with increased irritability of the large intestine," cannot be sharply separated from each other. The cause of these spasms has not been demonstrated. A great number may be functional, since they affect youthful persons and quickly disappear under suitable treatment, but naturally, in such cures we may have removed an external cause such as a change in food, removal of parasites (87), etc. In regard to the value of resection of the proximal colon, it must be remembered that retention of the feces in this portion of the intestine is purely secondary; such a procedure can, at the best, only improve the constipation by allowing feces to reach the distal colon in a less concentrated form, and this may act favorably on the spasm. The improvement shortly after operation is often deceiving, for the follow-up investigations of Rost have shown that the permanent results of cecum resection in this form of constipation are by no means brilliant. That present with gastric ulcer must also be classed as secondary (88). In this case, removal of the ulcer improves the constipation, but it returns when a new ulcer appears. Even if appendectomy in chronic appendicitis relieves the constipation, this also should be considered "secondary."

Furthermore, it has been stated that adhesions and veil-like coverings of the colon, especially of the cecum, are a cause of long lasting constipation. This condition will again be met in chronic peritonitis. On the proximal colon, these adhesions are called Reid's, Treve's, Lane's, Jannesso's and Jackson's membranes, or collectively, they are known as ligamenta varioforma (89). These fold-like formations of the parietal peritoneum may occur entirely without symptoms. As Eastmann says, a "large X," an unknown something, must be added in order that these membranes become troublesome (90). In some cases a colitis acts as an apparent exciting factor; but furthermore, as will be mentioned under chronic peritonitis, such veil formations may be the result and not the cause of chronic constipation. This can only be decided case by case after the results of operation are seen. Schlesinger (91) describes a stasis of the contents of the cecum below its junction with the ileum, resulting from such peritoneal adhesions.

Finally, a long lasting fecal stasis, 48 hours or more, in the proximal colon results when there is a diffuse atonic form of intestinal movements, that is, when the contents of all parts of the intestines are fairly uniformly delayed in their onward course. Under the x-ray, the colon is abnormally wide and relaxed. We do not know, at present, what disturbances of the innervation lead to such an atonic constipation. We are inclined to assume with Schmidt and Lohrlich (92) that there is an abnormally increased power of the colon to split cellulose, but it must not be overlooked that these writers found the same increase in the utilization of the food in

all forms of constipation, including the spastic. This too complete utilization can therefore only be a result and not the cause of the constipation.

Why is it that in all of these forms of constipation, the stasis of feces should occur in the proximal colon? Its reason, as Rost's anatomical investigations have shown, probably lies in that functional separation of the proximal and distal colon which has been discussed under normal colon motility. Rost showed by planimetric measurements of whole colons, and of the cecum resected on account of constipation, that there is no atrophy, but an hypertrophy of the proximal colon and it occurs in just those cases in which the feces had stagnated abnormally long in the proximal colon and in which this latter structure seemed relaxed and dilated ("typhlatoxie" (93)). This can only be explained by assuming that the actual site of constipation was distal to the cecum and the ascending colon, and that the intestines functioned against abnormal resistance, if there was not actual hyperfunction of the proximal colon in analogy to the animal experiments of Bohm, with vagus stimulation. It may be assumed further that the proximal colon can at first overcome the resistance, but later it must gradually fail.

To sum up, fecal stasis of long duration in the proximal colon, in the different types of constipation mentioned, must on the basis of what has been said, be considered purely secondary. This must be taken into account in attempts at surgical treatment.

That form, distinguished by Stierlin (84), as a transverse colon stasis, occurs when this portion of the bowel is ptosed and kinked at the splenic flexure (see under chronic peritonitis). But stasis occurs without the kink, and in these cases the anatomical investigations of Rost have shown that an atrophy of the muscle of the transverse colon is present and during life this particular form of constipation occurred. It cannot be stated, however, whether this atrophy is primary or secondary; it may easily be imagined that this transverse stasis is only an end result of a spastic constipation. At present, our x-ray pictures, are, of course, only isolated, and we are by no means informed of the processes involved in the development of constipation. This would necessitate observations of patients extending over years.

Finally a word must be added concerning the surgical treatment, which usually consists of the removal of the proximal or the entire colon. From the preceding statements, it is easily recognized that the pathological physiological conclusions regarding such procedures are not quite as simple as they appear. Hertz in speaking of the operation of Lane, who as is well known, resects the entire colon, affirms that Lane removes every healthy part of the large intestine and leaves behind the diseased portion

(proctogenic constipation), but it must not be overlooked that patients who are in a pitiable condition are often remarkably benefited by this operation. The only good explanation at present is that the elimination of some sort of toxic substances has been improved.

This leads us to the difficult and practically unsolved problem of chronic intestinal intoxication (see the remarks under ileus). Such substantial improvements have been seen after relief of constipation by resection of the cecum not only in high grade malnutrition, with its gray discoloration of the skin, but in cardiac disturbances, renal difficulties, numerous neurasthenic disorders, and changes in the blood picture, that it makes pertinent the assumption that absorption of toxic substances took place chiefly in this portion of the bowel. Operative procedures for constipation should be considered from this viewpoint.

As a third large division in the pathology of intestinal motility, the symptom complex known as ileus must be discussed (94). The four cardinal symptoms of this condition are retention of feces, vomiting of bile-stained or fecal material, meteorism, and abdominal pain. These sketch in rough outline this symptom complex, but to determine its exact boundaries has always been and will be its greatest difficulty.

The classification of those intestinal disturbances, which are collectively called *ileus*, is as varied as the viewpoints from which the question can be approached. If we adopt the pathological physiological facts as the basis of our classification, we must differentiate the obstruction due to mechanical causes from that of disturbances of any sort in the innervation (dynamic ileus), and we must further distinguish in mechanical ileus whether the blood vessels have also been obstructed (strangulation ileus or obturation ileus). Mechanical ileus is the easiest to explain. That the passage of feces should be impeded or checked completely when the lumen of the intestine is obstructed by a constricting carcinoma, or an impacted gall stone, etc. is naturally self evident. A stasis of feces must occur above the obstruction. Dilatation of the bowel and distention result and finally gases are forced back into the stomach and expelled by vomiting and eructation. We shall discuss the symptoms in detail later.

The conditions are not quite as simple in strangulation ileus because the obstruction to the circulation plays the most important part. On this depend all other symptoms of which, first of all, distention and meteorism must be mentioned.

In all forms of ileus, the explanation of meteorism has been considered easy. Gases and intestinal contents collect above the point of obstruction, evacuation cannot take place downward, new material is steadily added from above and distention must naturally result, its degree depending



on how far down the obstruction occurs (95). But clinical experience has shown that this explanation of meteorism does not apply to all cases, for meteorism not general, but localized and circumscribed, has been observed especially in strangulation ileus (96). The extensive experimental investigations of Kader (97) have enlightened us on this point, and our understanding of meteorism has been considerably improved. We must, according to these experiments, differentiate the meteorism in obturation from that in strangulation ileus. Every ligation of the mesenteric vessels (naturally also thrombosis or embolism), with its resulting stasis leads to a local meteorism, which forms quickly, and increases very rapidly. This meteorism, resulting from circulatory disturbance, paralysis and distention of the intestine, is very much greater than that resulting from simple obstruction of the lumen. But as we shall see presently, the paralysis and distention occur also in obturation ileus, and just as in strangulation ileus, are dependent on circulatory changes. This is of great theoretical interest (98), (18). The differentiation of strangulation and obturation ileus, as inaugurated by von Wahl, Manteuffel and Kader on the basis of the meteorism is, therefore, only an expression of gradual differences. In both cases, the circulatory disturbances are the essential causes, in practice, nevertheless, the differentiation of strangulation and obturation ileus, according to the degree of meteorism present, is quite justified.

In strangulation ileus, the muscularis of that portion of the intestine, the nutrition of which is disturbed, becomes paralyzed in a few hours, and the layers of the wall become edematous and hemorrhagic. These changes first affect only that portion of the intestine from which the circulation is cut off. The other portion, however, is also paralyzed reflexly, so that the same vigorous peristalsis is not seen or heard as in obturation ileus. This paralysis really corresponds more to that occurring in peritonitis for which, clinically, strangulation ileus is often mistaken.

There are many factors at work in the rapid appearance of meteorism after interruption of the intestinal circulation, that is, especially in strangulation ileus. In the first place, and this seems to be the most essential factor, the gas exchange between the blood and the intestines is impaired. As is well known, intestinal gases normally are composed of swallowed air and a mixture derived from decomposing food. Since carbon dioxide and oxygen are quickly absorbed, methane and hydrogen are especially found in the lower intestinal segments. These latter, and also nitrogen, are absorbed with difficulty. Sulphuretted hydrogen is present in such small quantities that its relation to meteorism is unimportant. The investigations of Zuntz and Tacke (99) have yielded most astonishing results; namely, that under normal conditions most of the gases in the intestines, indeed, even large quantities, are eliminated by the lungs after being absorbed in

the blood stream, and only a very small quantity escapes through the anus (proportion 10 to 1). A defective peristalsis, therefore, does not impede the elimination of these gases, but according to Zuntz, circulatory disturbances do, and of course in strangulation ileus, there is complete interruption of the blood supply.

However, all these statements do not explain why the gas exchange is lowered by passive congestion of the intestinal vessels; probably it is ultimately due to changes in the bowel walls themselves, since it cannot be assumed that the blood is carried away too slowly for this purpose. But it can be seen from extensive investigations (18) that absorption is diminished in the beginning of ileus; later it is practically abolished, and finally actual extravasation of fluid into the bowel takes place. These experimental findings correspond perfectly to clinical observations and explain, at the same time, why gases are contained only in that loop in which the circulation is impaired and why they do not escape to the adjacent parts of the intestines, which are apparently much less altered, but in which, obviously, the absorption is also much diminished.

As Hotz could show, the degree of paralysis of the bowel in ileus and peritonitis has a certain relation to the distention of the viscus. He found, when he isolated a loop of bowel, closed the central end and left the peripheral end open, that it was only the closed and distended loop that was paralyzed after peritonitis had begun, while the loops efferent to the section, and which had remained open, were not paralyzed. Furthermore, as Kocher (100) showed experimentally, distention of a loop of intestine has, in itself, caused circulatory disturbances so that there is a close reciprocal relation between meteorism, paralysis and circulatory disturbance, and it is easily comprehensible how one of these pathological processes can often influence the other unfavorably.

According to Pommer's (18) investigation, meteorism in circulatory disturbance of the bowel can result, not only from diminished absorption, but in another manner. In a case of thrombosis of the mesenteric arteries, he found an extraordinary massing of butyric acid bacilli in the bowel wall, which doubtless had found a very satisfactory pabulum in the disintegrating epithelium. Pommer believes that these gas forming organisms were responsible for the gases in this instance.

The paralysis in strangulation ileus finds its anatomical expression in edematous saturation of the musculature of the walls.

As stated above, the explanation of the occurrence of distention paralysis and circulatory disturbance in obturation ileus, must be essentially similar to that in strangulation ileus. But there are certain differences which are important, especially in the clinical progress of the former disease. In obturation ileus, the vascular supply is not so seriously involved in the

beginning, since the obstruction affects only the lumen of the intestine; nor is the distention so great, provided of course that the disease picture is not erased by peritonitis. The gases, at first, find areas in the intestines in which the absorption is still more or less normal; the dilatation occurs, of course, above the obstruction and remains the greatest in this part throughout the further progress of the disease. The distention of that portion immediately above the obstruction, can be explained chiefly by the increased current of fluid passing from the blood into the intestines. This increased secretion of fluid from the mucous cells is expressed anatomically, and the efferent and afferent bowel segment can be easily recognized microscopically from the appearance of the goblet cells (13).

As stated, the intestinal contents in obturation ileus are chiefly liquid (101), at least when the obstruction is of the small intestine; when of the large intestine, the gases predominate. This is especially interesting because, as we have seen, in discussing diarrhea, liquefaction is demonstrable particularly in the region of the colon. The complexity of the pathological processes is thus shown. If the obstruction persists, the distention may also become enormous; the musculature hypertrophies and not a short, but a very large segment of the intestine is dilated. In such cases, the difference in size of the afferent and efferent loops is very apparent at operation and in resection the suturing is made very difficult. Furthermore, after resection, such chronically diseased intestines do not recover very rapidly as the entire bowel has been affected. It has already been shown that circulatory disturbances resulting from the distention, occur at this stage. In strangulation, on the other hand, the normal activity is usually quickly re-established after resection, since the segments above the affected loop are paralyzed reflexly and not as yet from distention. This must not be overlooked, even if the disease picture in strangulation ileus is otherwise more dangerous because of the quickly supervening gangrene.

It has not been decided whether the meteorism in hysterical individuals is due to a paralysis of the intestinal musculature, or as Trousseau (102) assumes, to a spasm of the diaphragm with relaxed abdominal walls. If such a case is operated on, under mistaken diagnosis, it is most remarkable to see the meteorism disappear completely during the anesthesia.

The influence of the nervous supply of the intestines, in relation to the appearance of meteorism, is very little understood. Numerous observations have shown us, however, that there is a type of distention, which can only be considered due to a nervous reflex. Such cases are the intestinal distention at the moment of omental strangulation, twisting of the pedicle of intraabdominal tumors or organs, the meteorism in renal or biliary calculi, retro-peritoneal hemorrhages, mild abdominal injuries (103), and



many other conditions. The gaseous distention often amounting to ileus, which occasionally occurs after all sorts of aseptic laparotomies, also belongs to this class (104). It is usually assumed in these cases that the splanchnic nerve, that is, the inhibitory nerve of bowel motility, has been strongly stimulated reflexly. Whether this idea is correct has thus far not been examined experimentally. Reflex meteorism and reflex paralysis are only gradual differences of one and the same process. The impression is gained clinically, that the severe forms of this reflex paralysis presuppose a certain nervous disposition, but it must not be forgotten as we have said above concerning hysteria, that our knowledge of the actual cause of meteorism in such cases, is still very meager and uncertain.

After blunt trauma to the abdomen, as for example, a kick by a horse, the intestines are not usually distended shortly after the injury, but are, on the contrary, contracted and pale (Wilms (82), p. 81). Heineke believes that it is the tension of the abdominal walls, after intraabdominal hemorrhages or injuries to the intestines, which prevent distention of the latter structures. He concludes this from the observation in certain cases that marked meteorism was present in mild bruising of the abdomen. In these cases, no intraabdominal injury was present.

The meteorism which is occasionally seen in diseases of the central nervous system (tabes, apoplexy and that developing especially after fractures of the vertebræ) is generally held to be due to intestinal paralysis, but thus far there are no careful investigations regarding degeneration in nerves and ganglion cells. If the abdominal walls are also paralyzed another factor comes into play.

The separation of obturation and strangulation ileus relates only to the final condition; it often happens that an ileus begins as the obturation type and in the further course of events, that is, when the mesentery is also pinched, it changes to the strangulation type. The mechanism which produces strangulation ileus is not always easy of explanation. If we find, for instance, a large number of loops of intestine passed through a comparatively narrow ring, it may, in the first place, be caused by what we usually designate as "elastic incarceration." Under the pressure of the abdominal walls and forcible stretching of the elastic rings, as in an hernial aperture, a large segment of bowel is forced through. If the pressure within the abdominal cavity is reduced, the ring again contracts and incarceration is the result. The size of the incarcerated loop would then be proportional to the pressure in the abdominal cavity, and the diameter of the aperture. For conditions in a hernia, this mechanism is quite easy to understand, because low pressure exists within the hernial sac. This term "elastic incarceration" is now generally accepted in this condition,



especially since Ranke (105) reported a very typical case from Volkmann's clinic. But the conditions are quite different when loops of intestines slip through a ring within the abdominal cavity. Wilms (106) points with justice to the fact that the so-called intraabdominal pressure cannot be involved. There is actually no difference in pressure in the separate abdominal spaces, and if Kertecz (107) obtained different pressure readings by introducing a rubber ball into various parts of the abdominal cavity, it is obvious he was dealing only with measurements of the peristaltic power of the intestines. It is the peristalsis which plays the deciding part in the incarceration of large loops of bowel through some ring within the abdominal cavity.

All investigations and observations of suitable cases have conclusively shown that the further involvement of loops in such a ring is always at the expense of the efferent and never of the afferent segments. There is, however, considerable difference of opinion concerning the manner in which this pulling-in takes place, and this difference is difficult to remove because the intestines of the usual experimental animals, for example, the rabbit, do not have the peristaltic power of human intestines (106). Wilms believes it occurs in this manner: with enlargement, and stretching of the loop which is not at first incarcerated, and with a smooth constricting ring, more and more intestine from the afferent segment is pulled into the ring according to the law of lateral pressure. He attempted to support this view by experiments on cadavers ((106), p. 35), in which he pulled a loop of bowel through a smooth ring and injected fluids into the incarcerated loop. As a matter of fact, similar conditions occur in the living when the afferent segment forces fluids or gaseous contents into the constricted loop. Theoretically it can also be conceived that a similar mechanism has acted when a large loop of bowel is found pulled through a ring in ileus. Naturally it must be supposed that there was no incarceration at the beginning.

But how does the incarceration develop if the ring is wide enough to permit loops of bowel to pass through it in this manner? The principle is the same, whether the incarceration occurs inside the abdominal cavity or outside in a hernial orifice. When years and tens of years pass, and large masses of intestines lie in a hernial sac without being incarcerated and then suddenly the loops will not return to the abdominal cavity, without any stronger pressure having been applied, naturally the above mentioned form of elastic incarceration cannot be operative. In such cases, the term "fecal incarceration" is used. Many workers have dealt with this question experimentally (108). The experiments of Borggreve and Hessel, in which they placed a loop of intestines through a gap in the abdominal wall and then observed circulatory disturbances which

finally led to such edema of the bowel that the loop could not be returned, cannot be utilized in this connection, because the intestines came in contact with air. These conditions are entirely different from those occurring in ruptures. But the general importance of circulatory disturbances in incarcerated hernias must not be ignored on this account.

In the last century, during the forties, O. Bein performed an experiment which is really basic for all later experimentors. He cut a round hole, 1.5 cm. in diameter, into a piece of pasteboard and pulled a loop of bowel through the opening. If he blew air through a catheter into one end of the bowel, it escaped at the other end, but if he blew a large quantity in suddenly, none escaped and the loop of bowel became enormously distended. The method which Roser used in his well known and much cited experiment was somewhat different, but not new in principle. He pulled a loop of intestine through a ring, filled it half full of fluid and then attempted to empty its contents by sudden and forcible pressure. He did not succeed, even though the ring was fairly large, and Roser believed a fold-like formation at the level of the ring acted as a constriction. Many others have performed experiments in the same or similar manner (109). The results of all were the same, but the interpretation differed with the various writers. Thus Lossen believed that the afferent intestine would kink off the efferent loop as soon as the former was tightly distended, and thus no contents could escape. This idea has been much contested, probably with justice, and this mechanism in hernial incarceration probably does not play a large part in the living, even though Lossen, from these experiments on cadavers, devised a special method of taxis.

The application of these experiments to the living has always been in dispute since the contents of the intestines collected in this manner would have to be evacuated quickly into the afferent loop, thus releasing the incarceration. As further experiments then showed, a fecal retention resulted if in place of one hole, two holes are used through which the loop of intestine passes. A pinching off of the efferent through the afferent surely cannot take place in this experimental arrangement. Busch believed that the efferent loop was kinked off at the constricting ring, since, of course, the pressure on the convex side of such an arc shaped tube as the loop of bowel simulates in the hernial sac, is greater corresponding to its larger surface than that of the concave side. Consequently, the arc attempts to straighten out because of the increase in the internal pressure, and thus the efferent loop is kinked. But fecal incarceration results experimentally if the entire loop of bowel is placed in a funnel with the afferent ends protruding below. In this experimental arrangement, kinking is surely avoided. Karpetschenko therefore believes that a portion of the loop is occasionally twisted within the hernial ring and this leads to fecal incarceration.

In simplifying these experiments, new facts were discovered. Busch demonstrated that contents cannot pass if a simple section of bowel (no loop) is passed through a ring and then is distended, or if a segment of intestines is slightly constricted at any point, and then suddenly distended. Kinking, in the true sense of the word, does not occur in this case and Kocher then showed, with a slight alteration in the method, that distention of the lumen alone is sufficient to produce occlusion of the afferent loop. This occlusion occurs, as can be easily shown, through pulling some of the wall of the afferent loop, chiefly the mucosa, into the ring. This corresponds to the above mentioned lateral pressure. In this manner the entire lumen of the afferent end is occluded.

To briefly summarize, a so-called fecal impaction results if the bowel is constricted at any place by a ring, and quickly distended above this narrowed place. These experiments on cadavers have therefore taught us the manner in which a stasis of feces is brought about in a hernia. A stasis is, however, not an incarceration. The stasis of feces, would necessarily be relieved when a peristaltic wave relaxed, if other factors were not added. But that stasis persists is just the remarkable part of impaction, and to explain this, the effect of circulatory disturbances must be brought in. These develop in the manner described. We know that a circulatory stasis occurs in a short time after irritations of all sorts, and these disturbances once begun, naturally increase more and more. They probably also cause a simple stasis of feces to finally become an incarceration. How much this incarceration depends on circulatory conditions after ordinary fecal stasis is seen in the so-called "relaxed incarcerations" of old people, which, actually occur only in weakened circulation, as Wilms could show. In such cases ordinary fecal stasis persists for a long time, and it does not proceed to the incarceration which injures the bowel wall. The intestine is often found in such good condition even after three to eight days of incarceration that it is not necessary to resort to resection.

Circulatory disturbances therefore belong to the picture of incarceration, and they become especially severe when the mesentery also is kinked in intraabdominal strangulation ileus, or, if it is present in a hernial sac. Kocher, indeed, believes that there is still another form of circulatory disturbance possible. His experiments give evidence, though they are not conclusive, that distention alone can produce such severe circulatory disturbances, that hemorrhage and gangrene finally result. But an impeded venous outflow may lead to distention of the bowel, and his demonstration, that distention for two and a half hours leads to complete and permanent paralysis, is essential for the comprehension of the anatomical changes in circulatory disturbances. Paralysis of the



bowel, distension, and circulatory disturbances are therefore in close and causative relation, but thus far it is only known that circulatory disturbances cause all the others, and not *vice versa*.

Bands and adhesions in the peritoneum from previous pregnancy or from peritonitis, may cause ileus by the slipping of a loop of intestine under them; incarceration then results in the described manner. In the classic form of knot in the human intestines, such adhesions do not enter into consideration. Gruber and Wilms (110) showed that these knots occur because of a too long and too movable sigmoid flexure. The work of Wilms also goes into detail concerning the different forms which these knots may assume, and the conditions are made clear by a model made of tubes.

A most peculiar form of ileus is brought about by so-called retrograde incarceration. By this is understood that two loops of bowel find their way into a hernial sac without suffering very grave changes, but if the hernial opening is enlarged and the connecting loop between the two is pulled forward it is often gangrenous. Such cases have been described by Hoehenegg, Klauber, Lauenstein, Neumann, Sultan, Lorenz (111) and many others. The mesentery of the connecting loop was kinked in the hernial opening in only a very few of the cases; in the majority, there was no compression whatever of the mesentery. As Lorenz, among others, showed, the reason for the gangrene is in a peculiar kinking of the mesentery of the loop of intestine which is in the abdominal cavity. There is a certain similarity to what Wilms has called "twist closure." Lorenz could support his opinion by experiments on models.

Finally in mechanical ileus, the mechanism of invagination has been the object of many experiments. It is not difficult to produce them in animals, since small invaginations which usually resolve of themselves, are often found accidentally with otherwise quite normal intestines (112). That similar conditions occur in children during the agonal period, is also well known to pathologists. Nothnagel, Wilms and Knapp stimulated a segment of intestine with the faradic current and observed the formation of a local point of contraction which was then roofed over by the relaxed distal segment, somewhat like an umbrella. Finally, an invagination of the contracted portion into the relaxed portion occurred. These invaginations usually resolve themselves in a very short time. Propping and Knapp readily obtained similar invaginations by the injection of physostigmin. There is, however, still some difference of opinion in regard to the manner in which the longitudinal musculature participates, if at all.

A prolonged invagination, as it occurs in man, cannot be obtained in animals, at least, only by complicated methods which correspond little to natural conditions (113). If, as Knapp states, these experimental



invaginations occur through stimulation of the ends of the vagus nerve in the intestines, observations of invaginations in individuals with vagotomy would be of especial interest. That the ileocæcal valve is not the part where invaginations begin, as it was formerly assumed, has been discussed under Bauhin's valve.

The classical example of "paralytic ileus" that is, obstruction resulting from paralysis, occurs in peritonitis. In general, the assumption is made that it is a toxic effect on the ganglion cells which lie in the walls of the intestine. That this view is too simple has been shown by the investigations of Hotz (98), who found that intestinal paralysis in peritonitis occurs only in the distended segments, and those which are not distended, but which are equally involved in the inflammatory process, retain a quite normal motility. According to this, it seems probable that the distention and the paralysis are also indirect results of circulatory disturbance in this particular condition. Since, according to the investigations of Enderlen and Hotz (18), the absorption from the intestine is decreased in the early stages of peritonitis and ileus, while later there is considerable more fluid excreted into the bowel, we observe, in every pronounced case of these diseases an enormous accumulation of fluid in the lumen of the intestines, and this, together with the gases, leads to further distention. There results, according to the above statements, a severe, and eventually irreparable circulatory disturbance, and later, according to Hotz, paralysis. The surgeon, therefore, in operations for ileus or peritonitis must assume the task of removing these abnormal fluid and gaseous masses which have collected in the bowel. Evacuation is the first consideration in the treatment, and an astonishingly quick recovery of an apparently paralyzed bowel (for example in incarcerated hernia) is often seen after the bowel has been emptied by stripping during the operation. Fistulæ often act in a similar manner, but are naturally less completely effective (114).

Still more difficulties are presented for pathological physiological analysis, by the lighter grades, in which there is no pronounced obstruction to the intestine, but only a certain inhibition or irregularity in the peristaltic movements.

Spastic ileus in which there is obstruction to the passage of intestinal contents through prolonged contraction of various segments, presents a contrasting picture to the paralytic type. From the pharmacological viewpoint a paralytic ileus would correspond to that resulting from adrenalin while spastic ileus corresponds to the action produced by pilocarpin. The most important practical example of spastic contraction, resulting from poisons, is that due to lead. The spasm observed in the presence of ascarides in the intestines, also depends on the action of a poison (87).

Those seen with ulcers or fissures are usually considered as reflex. Others occurring in the presence of foreign bodies, for example, small calculi not obstructing the lumen, are usually placed in the latter category. Such contractions rarely produce ileus, but it does occur occasionally (for example, in the presence of ascarides (87)). Unquestionably, they occur in certain individuals more readily than in others, as we have seen under fissures where there is an extensive painful spasm of the entire large intestine. A nervous disposition is spoken of, based on the occurrence of spasm in hysterics, in which disease they may supposedly be sufficiently severe to produce ileus. The difficulties in understanding how contraction of a small segment can offer an absolute obstacle to the passage of feces or gas, have been emphasized often enough, but it must be remembered that in circumscribed spasms, we do not know what movements this segment and those in its vicinity carry out, or what disturbances which cannot be observed fluoroscopically, the other loops of intestine undergo, but which may be able, nevertheless, to produce obstruction. Something like this occurs in *ascaris* ileus (Rost).

Probably the highest degree of spasm is observed in tabes, in which it occurs over large areas. Indeed, Schlesinger (91) describes a case in which the entire descending colon contracted to a tape-like form at a time corresponding to a crisis.

A special form of circumscribed meteorism was first described by Maydl and Bayer (115). In this condition, the cecum becomes distended, balloon-like, after deep seated obstruction of the bowel. It may reach a degree severe enough to produce ulcers from stretching, which finally may perforate and cause death from peritonitis (116). An essential in the formation of this isolated distention of the cecum, is an air tight Bauhin's valve. Furthermore, the investigations of Anschutz (117) and von Greyerz have shown that the thinness of the wall and the relative width of the cecum are the causes leading to the greater distention of this part. The former illustrates the conditions very well by a schematic investigation which has often been confirmed (Greyerz). He tied two rubber balloons of unequal size to a "T" tube and blew air through the third arm. The larger balloon expands very quickly and bursts before the smaller balloon has reached any noteworthy size. Kreuter, indeed, has doubted that the interpretation which Anschutz gives to this experiment is correct, but the mathematical calculations of A. de Quervain (reported by von Greyerz) have shown that "with membranes of equal elasticity, the pressure is higher when the radius is smaller; therefore, that degree of pressure which will suffice to distend the membrane with the larger diameter, will not be sufficient for the smaller." Consequently, it cannot very well be doubted that the greater diameter of the cecum, as compared

to other portions of the colon, is the reason for the exceptional distention of this part. Clinical observations also support this view. In rectoscopy, for instance, when air is blown from the rectum into the colon, the patients usually complain of pain first in the region of the cecum. There must be the greatest amount of tension here, of course, since it is the end of the tube. Attempts have been made to utilize this pain in the region of the cecum as a diagnostic sign in appendicitis (118), but it is naturally not pathognomonic and is useful only in isolated cases (see 119).

The formation of ulcers above an obstruction must be regarded as the mechanical result of severe distention. They are usually small and rounded and often present in large numbers; their former description as "decubitus or stercoral ulcerations" (Nothnagel (112) p. 183) indicated the view that they were produced by the pressure of stagnating hardened feces. But Kocher (108) has correctly pointed out that thick or solid feces are not present in ileus, but fluid and considerable gas, and, therefore, the contents of the afferent loop are soft. As a result of his investigations in incarcerated hernias, he considers them the result of overstretching. The distention of the intestine leads to a disturbance in the nutrition of the wall, and this to a circumscribed ulceration and gangrene, both of which processes are favored by the omnipresent bacteria. According to the later, extensive experiments of von Greyerz and von Shimodeira (120), there is a diminution in the arterial blood flow very soon after distention makes its appearance. The intestine becomes pale and ulcers may appear even at this stage. After the distention is released, the intestine becomes deep red in color, a sign of venous stasis. Kocher and Prutz (121) in their first paper at least, also consider this venous stasis and its resulting thrombus formation and hemorrhage the essential reason for the formation of these ulcers; but it is really very difficult to arrive at a certain conclusion. The explanation of such anatomical findings, as reported by Prutz, is indecisive, because it is never known whether they are primary or secondary. The fact that experimental ulcers occur only after four to five days following distention with air, as described by Shimodeira, really seems to point to nutritional disturbances of the intestinal walls through venous stasis. And now paralysis of the intestine may follow the circulatory disturbances as has been discussed in detail above. In addition, the absorption of gas is limited, and this in its turn, leads to the development of meteorism. There is thus created once more a vicious circle, which requires that the contents of the intestines be emptied as quickly as possible.

Further results of distention, as it occurs in ileus, are increases in intra-abdominal pressure; from this standpoint the same pathological physiological conditions arise as in ascites. In Hamberger's investigations of the influence of intraabdominal pressure on absorption, the question of



blood pressure was also considered (17). He increased intraabdominal pressure by injecting physiological saline solution and attempted to eliminate the elasticity of the abdominal walls by placing a plaster of Paris cast around the abdomen of the rabbit. At the beginning of the increase in intraabdominal pressure, he observed an increase of blood pressure, but when it reached high levels there was a sudden fall in blood pressure followed by death of the animal. Hamberger's investigations were confirmed in their most important parts by Qurin (122), who used air instead of saline solutions. Oppenheim (123), who pumped air into the lumen of the intestines and produced high grade meteorism, also observed a marked failure of cardiac action, leading, in certain cases, to quick death. These writers interpret the results of their experiments, as follows: "When pressure is exerted in the abdominal cavity, the circulation, especially that in the veins labors against increased resistance." The results of this condition are first, increase in the blood pressure and second, when the resistance becomes too high, complete failure of the heart with a fall in blood pressure, and death. But Stadler and Hirsch (124) criticised this interpretation. They also determined the blood pressure after increasing the intraabdominal pressure by blowing air into the anus. They obtained a true meteorism. They also found the primary rise in blood pressure, but demonstrated that it was synchronous with difficulties in breathing from elevation of the diaphragm which with displacement of the heart could be seen with the *x*-ray. In violent dyspnea, a vagus pulse was noted, but they never observed the fall in blood pressure which Hamberger obtained. This fall was explained by saying that the inelastic plaster cast finally caused a complete compression of the large veins and thus the heart secured no more blood to pump. The heart fails, therefore, not because of an increased resistance, but because it contains no more blood upon which to act. But the researches of Hamberger are interesting from the standpoint of the surgeon, because severe disturbances in breathing and heart action are occasionally observed when large plaster casts are placed too tightly around the abdomen, especially when intraabdominal pressure increases after partaking of a meal, or in conditions of distention. In applying these casts, this should be remembered, and an abdominal pad placed in such a position that it can be removed when the plaster has hardened.

The stagnant contents in the paralyzed and distended loops are said to lead to an intoxication of the organism (*auto-intoxication*). This question of auto-intoxication, arising from products within the intestines has played a very large part in the literature. Metchnikoff has given this question its most popular form in his book on an optimistic world philosophy, which finally culminates in the recommendation to use Yoghourt-



milk (sour buttermilk) which by cleansing the intestinal tract, diminishes the intoxication and is said to insure long life. We will confine ourselves in this discussion to that occurring in ileus, since the conditions are the simplest in this disease. The special question to be decided is whether death in ileus is actually a result of such an intoxication as is frequently asserted. The theory, which unquestionably is very attractive, was first put forth by Amussap in 1839, and later by Humtert, Bouchard, Albu and many others (125). From the surgical side the practical deduction was drawn, that toxic intestinal contents must be removed in ileus through enterostomy in the quickest possible time; undoubtedly this was an enormous step forward in the treatment of ileus (100), (114), (126). Enterostomy, however, owes its favorable influence to other reasons, as was discussed above *viz.*, because it removes the tension in the loops of intestines, as Heidenhain pointed out.

It required many experiments to decide the importance of auto-intoxication in ileus; the works of Nikolaysen, Nesbieth, Kukula, Albeck, Borszky and Genersich (127) may be mentioned. The plans of these investigations were all more or less similar. The writers produced an intestinal obstruction in animals in various ways (a procedure which is not always easy), they sterilized the contents by filtration or heat, and injected into other animals, either intravenously or intraperitoneally, the filtrate or even the gases formed in distended loops. Several also used intestinal contents from human cases of ileus. The investigators then obtained, with considerable uniformity, certain signs of intoxication, usually followed by the death of the animal, which they emphasize, is similar to the death occurring in ileus. The next step was to isolate the toxins from the intestinal contents, and this led to the conclusion that they were probably of bacterial nature, but other substances, such as sulphureted hydrogen, phenols, etc., were isolated, which also produced severe symptoms. They were evidently not due to neurine, proteoses or peptones, substances which might occur to one (128). It was indifferent how they were applied, these poisons always produced the same results if the proportion to body weight was properly chosen.

The fact must be borne in mind that these experimental procedures were not sufficient to decide the question, because they only tell us that certain poisonous products are in the obstructed intestinal contents, and do not decide that they cause the death of the animal. It must first be shown that such poisons do not exist in normal intestinal contents, or that they are present in a considerably smaller quantity. But this demonstration has not been carried out with sufficient detail in any of the works quoted, as Braun and Boruttau (129) point out. Albeck, it is true, mentioned that, in his experiments, the injection of normal intestinal

contents only occasionally, but that of strangulated loops, almost always caused death, or at least grave symptoms, but the very careful comparative results of Garnier (130) are in contrast to these more or less doubtful statements. The latter found on dilution of the stagnating contents, that there was no difference in the toxicity of the normal and obstructed material. Further experiments of Braun and Boruttau confirmed these results, indeed they showed that the injection of similarly large amounts of the contents of normal bowel, and strangulated loop would occasionally be withstood. A great deal depends on the portion of the intestine from which the contents were taken, at least, the studies of Roger (131), Magnus-Alsleben, Falloise, Braun and Boruttau, show that the contents of the duodenum are by far the most toxic, possibly because of the large quantity of enzymes they contain. Conversely, the contents of the colon are the least toxic. This corresponds quite well with an observation of Clairmont and Ranzi, that intestinal contents lose their toxicity on prolonged standing.

If proof, that stagnant intestinal contents are more poisonous than normal is not forthcoming in these experiments, there is nevertheless the possibility that the toxins unquestionably present in ileus, are absorbed more rapidly than under normal conditions, and may produce their damage because the organism cannot keep pace with its splitting of the poison. Clairmont and Ranzi have studied the absorptive processes in ileus in the following way: an obturation ileus was produced and at various intervals laparotomies were performed and iodide of potassium injected into the dilated loop; the excretion of the iodide was then determined in catheterized urine. They believe these experiments showed that there is an increased absorption at first, but later it is delayed. However, as Braun and Boruttau emphasize, only the time elements have been considered in these investigations, and this gives a false picture of the magnitude of absorption. In place of the potassium iodide, these workers therefore, injected a crystalloid poison (strychnin), and then they showed, in the first place, that it requires a much larger quantity of the poison, to produce convulsions and death, when this substance is injected into a distended loop, and secondly, the convulsions and death in ileus occur later than under normal conditions. "The intensity and rapidity of absorption in ileus are as a rule immediately and increasingly diminished." Finally Enderlen and Hotz (18) in very extensive experiments, studied the same question in both ileus and in peritonitis. They found that absorption is diminished quite early in ileus and ceases almost completely soon after. In peritonitis, the absorption is unchanged at the beginning, but in the later stages it is greatly diminished.

Furthermore, the question arises, is the experimental disease or its course similar to that observed clinically in man? This cannot be

answered positively. A striking difference is this, the animals in experimental poisoning from intestinal contents die in convulsions, while this symptom, as is well known, is very rare in human ileus. The same phenomena are observed in animals even when the poison has been injected very gradually or in small quantities over longer periods. Furthermore, careful examinations of the blood pressure and respiratory curves in the ileus animals, and in the animals who have received injections of intestinal contents, show that they have not the least similarity (Braun and Boruttau). The statements that the animals die after the injection of intestinal contents, with the same symptoms as those observed in ileus rest therefore on inaccurate observation.

McLean (132) has attempted to solve this question in a somewhat different manner and by a more suitable method. He removed blood from dogs suffering from ileus and injected it into others. Even with this procedure, no symptoms of intoxication developed, and he transferred almost the entire blood in a number of instances. Thus we may sum up by saying that, thus far, there is no proof that the death from ileus is due to an intoxication from stagnating intestinal contents. Furthermore, Sauerbruch and Heyde's experiments (133) on animals, which had been previously sewed together "parabiotically" also have not demonstrated the presence of a more severe auto-intoxication in ileus. The fact that after ligation of the intestines in one of the animals there was a rise in the temperature of both, is too ambiguous, and cannot be used to show the cause of death in ileus.

Another group of authors believe that the clinical course of ileus is a bacteremia. We shall discuss the permeability of the intestinal wall for bacteria in the paragraphs on peritonitis (paths of infection of the peritoneum). Bacteriological examinations of the blood and peritoneum in experimental ileus have been made particularly by Albeck, and Borszeky and von Genersich (127). As could be expected after what was said in relation to peritonitis, no constant success attended their efforts. Bacteria could be demonstrated in the blood in only about half of the cases, and in the peritoneum, only after quite severe injury to the intestinal wall. Clinically, ileus is not a septic process, even though a great number of these patients finally die with the same symptoms as those of peritonitis, namely, circulatory failure. Death from ileus might therefore be considered similar to that from peritonitis, but the question of the fundamental cause of the circulatory disturbance must be left open. Pathologically anatomically, the infection of the peritoneum in ileus is often not very severe, but then in peritonitis also, the severity of the symptom complex by no means depends on the pathological anatomy. As a matter of fact we do not know on what it does depend.

The clinical course of the disease differs so essentially from that of peritonitis that there must be something exceptional. If auto-intoxication is not probable on account of recent researches, then it still remains an open question what this remarkable something is. The investigations of Kirschstein (134) and Reichel (13) are of especial interest in relation to this point. They found that if the small intestine is cut through and the end closed, it was possible to keep animals living for six weeks without ileus developing, the animal's final death being due to increasing loss of appetite and starvation. From these experiments we see that the whole symptom complex which we call ileus, that is, vomiting, wasting, liquefaction of intestinal contents, etc., is not a simple mechanical result of intestinal obstruction. Reichel believes his experiments indicate that there is either a reflex action from a strangulated intestinal loop, or peritoneal inflammation at the basis of the whole process.

It is obvious that extraordinarily complicated pathological physiological processes are concerned in this problem and we are still unacquainted with the details.

[Sweet and his collaborators (SWEET, J. E., PEET, M. M. and HENDRIX, B. M., *Ann. Surg.*, p. 721, 1916) have called attention to the clinical similarity, between high intestinal obstruction and acute pancreatitis. From experiments in which they considered the presence or absence of pancreatic juice, they are led to conclude that without its intervention, the acute toxemia of intestinal obstruction does not occur. This would explain the fact that closed loops of ileum do not give toxic symptoms. That is, animals in which a blind end of the duodenum longer than 35 cm. from the pylorus is made, live, while if it is less than 35 cm. the animals die. Whipple and his associates working on the same problem were able to isolate a highly toxic substance of the nature of a protease, from isolated loops. They believed it is formed in the intestinal loop, or from, or by the mucosa. Sweet believed the proteolytic ferment of the pancreatic juice is concerned in its appearance. Whipple however, has demonstrated the presence of toxic proteases in the exudate of peritonitis (WHIPPLE, G. H., *J.A.M.A.*, 67, p. 15, 1916).]

An important diagnostic sign in ileus, is ringing and tumbling noises in the intestines which are occasionally somewhat similar to the noise produced by the emptying of a bottle. They appear at the end of a colicky pain and are caused by the back flow of fluid contents and gases from the obstruction. The metallic ring indicates tension, and is due to bubbles rising in the fluid contents, or to drops falling back from the wall onto the surface of the fluid. They have been studied experimentally by Wilms and Leuenberger (135).

Manipulations of the intestines and of the peritoneum, may lead to what we designate as *shock*. This expression is a collective idea. In the



first place, the shock of anaphylaxis must be differentiated from so-called surgical shock, even though the possibility exists that further investigations will show a certain similarity in their clinical symptoms. Experimentally, anaphylactic shock can be produced by a series of proteins, peptones and histamines. The cause in this case is an alteration in the blood distribution. As the investigations of Mauthner and Pick have shown, there is a constriction of the blood vessels both of the liver and the intestines. During the contraction of the liver capillaries, the venous blood in the intestinal vessels is choked back (136). A constriction also occurs in the capillaries of the lungs. Blood pressure falls because the heart receives nothing to pump.

This fall in peripheral blood pressure is the most prominent sign in the shock after abdominal operations. According to the opinion of Crile (137), and Mummery (138), the blood pressure sinks because of paralysis of the vaso-motor center. But numerous investigations of other writers, such as Malcolm (139), Seelig and Lyon, Mann (139), have shown that the blood vessels in shock are not dilated but constricted. This applies equally to those of the abdomen. There is thus this remarkable similarity to the constriction occurring in anaphylactic shock. As stated, unquestionably the fall of blood pressure is the most prominent sign. Its cause is not known with any degree of accuracy; that influences which lead to shock, act on the central nervous system seems very probable. It is possibly not entirely incorrect, to consider with Brown that shock is caused at times by the anesthetic and at times by pain sensations which reach the nervous system unconsciously, notwithstanding anesthesia (140). He considers shock, after operation, a condition of general exhaustion of the nerve cells. It cannot be denied that this is a very pertinent idea, for it is an old experience that fatigued patients are poor operative risks, as for example, soldiers exhausted from severe physical or psychic strain, of which Nelson's surgeon in the naval engagement of Trafalgar has already spoken. Ordinary hospital experience also shows how much the post-operative course depends on psychic factors, on the energy, and on the courage of the patient. But how these things are related to each other in detail is not at all clear.

Other theories have been proposed to explain the different clinical symptoms of shock. Yandell Henderson (141) sees an essential factor in carbon dioxide impoverishment of the blood, and he believes that if the intestines are strongly stimulated in abdominal operations, breathing is more rapid and deep and thus the carbon dioxide of the blood is blown off and the natural respiratory stimulant diminishes. Cessation of breathing is therefore said to be the primary factor in shock. The blood pressure would fall later. Among others, Janeway and Ephraim (142)

subscribed to this opinion, but Short (143) on the other hand, has been unable to demonstrate a diminished carbon dioxide during surgical shock. Cobbet and Valte (144), in their theory of oligemia, see an increased viscosity of the blood as the cause of shock. Once again, Short could not demonstrate this condition. According to the opinion of Bainbridge and Parkinson, the cause of shock is to be found in an exhaustion of the adrenals, but later investigators on this particular question have arrived at varying results, although the theory enjoyed fairly extended acceptance. The least that can be said of these last mentioned theories is that they were probably too precipitate in their conclusions. It is better to first collect a plentiful amount of data, both from observation and experiment, and when this is sifted, begin to construct definite disease pictures. The future must decide whether surgical shock should be considered one or many diseases.

[Cannon, after considering the results of observations and experiments during the war and correlating them with previous knowledge, has written a critique which well covers the ground (*J. A. M. A.* 70, p. 611, 1917; 70; see also *J. Lab. and Clin. Med. Edit.* 21, 6, p. 405, 1920].

The *mechanism of intestinal injuries* from the application of blunt trauma to the abdomen has been well studied both clinically and experimentally, so that there is complete harmony in the views of the essential points. The magnitude and the direction of the force, as well as the place on the abdomen to which it is applied, determine the type of injury. The mechanism in both stomach and intestines is quite similar and may be discussed jointly under the classification of contusions, ruptures, and tears by pulling forces (145).

An injury from crushing is produced, as Morgagni (146) has described, when the anterior abdominal wall is pressed inward with such force that the intestine is caught between it and the vertebral column. The abdominal wall itself is not injured probably because of its anatomical structure, on which Longuet and Beck (147), lay particular stress, but even more so perhaps, because it is not squeezed directly against the bone, the bowel acting as a sort of shock absorber (148). It follows that crushing of the intestines is less likely to take place under a tense abdominal wall than under one which is relaxed, and actually it is not possible to produce this type of injury, by a blow on the taut abdominal walls of a dog tied up with his hind legs extended.

This idea had been forgotten for a long time until Longuet, on the basis of an experiment, again formulated and proved its worth. Later investigators (149), who worked either on cadavers or animals, found that the falling blow must be directed against the vertebral column or the iliac fossa; if it was struck over a larger area, only those loops were torn which

had previously been fastened to a bony base (Curtis). It was not necessary to hit the median line or the region of the ileum, but the direction of the force had to press the abdominal wall against the underlying bone.

Furthermore it was found, that the loop of intestine must be filled, not with air since that is compressible, and tears could be achieved only with difficulty (Curtis), but with fluid or hard feces when it is still more endangered on account of the greater circumference, thereby differing from ruptures, which will be discussed presently. Hertle (150) in his studies of the anatomical picture in crushing, found that mild injuries tear only the serosa and perhaps the mucosa; the muscularis and the submucosa remain intact. More severe trauma tears all the layers, but the serosa and the mucosa are usually split over a greater area.

For rupture to occur, it is necessary that a closed space be formed by kinking, displacement or adhesions. The intestinal contents then can not escape into an adjacent loop at the moment the force is applied, but must exert pressure from within outward when the space is suddenly reduced. In the pure cases, therefore, the rupture does not occur at the place where the blow falls, but distant from it. This conception has given rise to many doubts (151), but Hertle attempted to demonstrate its possibility by allowing water to flow through an excised loop of intestine and then rupturing it by a blow with his fist. Human findings, appear more conclusive, that is, there have been cases reported, though few, in which the rupture is distant from the place on which the blow fell, and in which a crush can be entirely excluded (Hertle). The opinion of Kempf (152), that the air compressed by a blow expands with such power when the force is removed, that it ruptures the bowel from within, requires considerable experimental support. As a matter of fact, pure rupture is probably a rare injury, it is usually combined with crushing, as exemplified in the critical references to the cases reported by Petry (153), Sauerbruch, Bunge, Hertle and others. By overdistention of the large intestine with air, a purely mechanical rupture may be obtained. Clinically, this may happen when the organ is inflated for diagnostic purposes in the presence of ulceration; and such injuries have been described as occurring in industries which use compressed air (154) (14 cases of rupture of the sigmoid). Anatomical investigations have shown similarly, that the serosa and then the mucosa is torn, while the submucosa seems to be the most durable and remains intact until the last (Hertle). With certain precautions, therefore, conclusions of the type of injury may be drawn in a given case, since in crushing the musculature is always torn first while the serosa is equal in its resisting power to the submucosa, but is much less so in distention. Particular interest has always centered around those tears which occur from severe and violent exertion, chiefly

compression without the application of outside force. Since the pressure within the intestine, and that acting on the abdominal wall from the outside, run parallel, a bursting rupture can only occur when there is a circumscribed place in the abdominal wall which is elastic, that is, in hernias (Bunge). Then a series of events well known to automobilists follows; if the casing of a tire is defective at one place and the tube is blown up very tightly, the latter first forms a small projection into the defect, and finally blows out. The bowel ruptures in a similar way under strong pressure, if a portion of its wall can force itself through a hernial opening. The peculiar tears of the rectum during violent abdominal compression, have also been explained by Bunge's deductions. Here, Douglas's cul-de-sac, that is, the place through which the rectum passes through the levator ani, is the weak point into which the small intestines are forced; the rectum stretches, and finally tears. It is a fact, that tears in the rectum are found exactly at this place, and loops of small intestines often lie in the rectum. Furthermore, such injuries are found more frequently when there has been a previous prolapse.

The mechanism of pulling has been expressed as follows: (Strohl in 1848) (155), "if an elastic body is to be torn, it must be fastened at one end and be pulled away from the place of fixation by some force" (148, p. 140). According to A. Neumann (156), the force may be applied either perpendicularly or parallel to the axis of the intestines, the difference being in the direction of the tear, especially that of the mesentery. Among the causes of this form mentioned in the literature, are fall from a height, kick from a horse, being run over, blow from a wagon tongue, etc. The direction in which the force exerts its action is the important factor in all; thus, Sauerbruch produced separation of loops of intestines from their mesenteries in cadavers, by delivering a blow against the abdomen from the side. Hertle explains the action of pull in being run over, in this way; the intestine is caught through the abdominal wall by the wheel somewhat like a brake, or the intestine folded against the mesentery becomes stretched and tears at its point of fixation. Petry (153) describes a case in which he could analyze the direction of the force and its pulling effect by the traces left by a hoof on the sigmoid flexure. Anatomically, injury from a pull is characterized both by sharp margins which show no crushes and by the oblique and transverse directions which the tears take. In a fall from a height, a pulling force is exerted on the intestine, because similar to the rest of the body, the loops of intestine participate in the energy of movement. This momentum is still in action when the body strikes the ground, and is brought to rest. A transverse tear is the natural consequence, occurring usually at the highest loop of the jejunum, near the duodeno-jejunal flexure, which, being fixed, does not yield to



the pull. In cases of being run over, an occasional result of the pull is a circumscribed stripping off of the serosa (Hertle).

The gravity of the peritonitis following, depends on how high a loop was injured, and on the amount of intestinal contents which escape. In transverse rupture, only a small amount will be present in the abdominal cavity if the patient has not consumed much water, chiefly because the mucosa rolls up and plugs the opening (157).

Apart from the primary peritonitis, hemorrhage and gangrene are to be feared because of involvement of the mesenteric vessels. The latter may also occur without injury to the intestines (158), as Eichle demonstrated experimentally, but little can be added to the statements above concerning their mechanism. If the bowel is stretched (bursting mechanism), it may be torn from its mesentery immediately at the point of attachment and in a direction parallel to it. These injuries are often considered less important than those affecting the intestines themselves, but the mortality of unoperated cases, is very high (159). As cases of Aldrich and Matthes (160) show, hemorrhage does not always begin at once, but may make its appearance days after, although the latter event is rare.

Free hemorrhage into the abdominal cavity is always an indication for surgery. That a puncture of the epigastric artery by a stab wound, may lead to a pouring out of blood into the abdominal cavity, is not difficult to understand. Hematomata readily form in the leaves of the mesentery after blunt injuries; if chylous vessels are also injured, a so-called chylous ascites develops; a late consequence may be a chylous cyst. These hematomata, may, by pressure on vessels, produce secondary gangrene of the intestines (161).

Blunt injuries, that is, crushes, are occasionally produced by attempts to reduce strangulated hernias by taxis. Rarely, but still occasionally, the mesentery is injured by the application of a Momburg tube. Verth (162) among others, reports a case in which, after prolonged constriction, there occurred a severe injury to the mesenteric vessels, which was the direct cause of death.

The results of injury to larger vessels in the mesentery cannot be separated in their pathological physiological results from thrombosis and embolism, since the injuries sustained by the intestines, through such lesions, are exactly similar (163).

Litten's (164) investigations have shown that *ligation of the main trunk of the superior mesenteric artery* in animals is always followed by extensive intestinal infarction, from which the animals die. After the ligation, the intestines become bluish red, are saturated with edematous fluid, and become thickened. Blood leaves the vessels and enters the

surrounding tissue, and this increases the discoloration. In other words, there is that accumulation of blood in the loops of intestines, which we call hyperemia; but why is it that blood accumulates in the loops of bowel which have been robbed of their arterial blood supply? Litten adopted the same opinion held by Virchow and Beckmann and Cohnheim (165), who believed that hemorrhagic infarction after ligation of an artery is a result of venous back flow, since no pulsation could be demonstrated either in the mesentery or in the bowel, even up until the death of the animal. But Cohn, and von Recklinghausen (166) considered this explanation insufficient, because hemorrhagic infarction was just as pronounced, or even more so, when the vein, in addition to the artery, had been ligated. They believe there is an inflow of arterial blood from the margins of the infarct. Litten indeed, had demonstrated that there were anastomoses between the inferior and superior mesenteric arteries at the margin of the intestines. The superior mesenteric artery is, therefore, anatomically, not an end artery, but since such severe nutritional disturbances result after its ligation, Litten calls it a "functional" end artery. A sufficient increase in pressure in the inferior mesenteric artery is not developed to fill the collateral channels. But this idea is somewhat misleading, because the experiments of Bier (167) have shown that a marked increase in pressure occurs only when both carotids are ligated, while usually the development of a collateral circulation after ligation of any artery, is not dependent on an increase of blood pressure.

The mechanical conditions for forming an anastomosis are more favorable in the case of the inferior mesenteric and the celiac arteries. Ligation of their trunks, therefore, leads only to a passing hyperemia and not to a necrosis of the intestinal wall.

The whole question entered into a new phase with the observation of Sprengel (168), that occasionally, although rarely, an anemic infarct may occur in the intestines. Niederstein (169), under Sprengel's direction, studied the conditions under which such an infarct arises. They believe that for an anemic infarct to occur, it is necessary that thrombosis of the veins be produced in addition to obstruction of the artery. The technic, which Niederstein used, in addition to ligation, consisted of the injection of paraffin into the vessels. The conclusions, however, are not entirely convincing, and objections, such as those of Marek (170) cannot be put aside. The latter worked independently and almost at the same time as Niederstein, who did not take into sufficient consideration—indeed he could not with his technic—how great a part the paraffin played in blocking off the arterial anastomoses. Marek, on the other hand, could show accurately that to produce an anemic infarct of the bowel, it is sufficient to interrupt all the arterial blood supply. According to him, it

is quite indifferent in the production of an anemic gangrene, whether blood coagulation took place in the veins or not. With this, the question of why hyperemia occurs, when the mesenteric artery is obstructed, is very probably decided. Arterial inflow, through the anastomoses, is essential. A venous backflow only increases the results of the arterial collateral supply, but can never suffice alone to produce hyperemia in an isolated segment of the intestine which has had its arterial supply completely interrupted.

Bier has attempted to explain the reason for the formation of a collateral circulation after occlusion of one of the main arteries, by stating that the smallest vessels in the anemic area dilate automatically, that is, independently of the central nervous system, and suck up the blood, as it were. There seems also to be a certain selective action, especially among peripheral arteries, in that the vessels are closed to a venous backflow, but are open to arterial blood, thus, automatically sucking this nutritive blood into their lumina. This faculty of the small vessels, is supposed to be developed more poorly in the intestinal vessels than in those of the extremities.

Ligation of the trunks of the *mesenteric vein* is also followed by hemorrhagic infarction but ligation of isolated branches leads only to stasis, the blood quickly flows into the abundant collaterals, and no lasting injury results. If, the main trunk of the vein is ligated and collateral circulation rendered impossible, the congestion in this area becomes more and more pronounced, as the artery continually adds blood, until the overloaded small vessels rupture and blood escapes into the tissues. Hemorrhagic infarction and later gangrene are the natural consequences. In man, ligation of the superior mesenteric vein, is always followed by a fatal infarction. The contrary statement of Mayo Robson (171), in which he believes that he ligated the main branch of the superior mesenteric vein without the death of the patient, is doubted by Wilms (172) since, judging by the position of the wound in this case, it appears impossible that an injury to the main trunk of this vein was produced. It can be reached only behind or above the pancreas. Of course, there are occasional anatomical anomalies which might permit of sufficient collateral circulation after ligation of this vessel, but they must be rare (see 159, p. 221).

Thrombosis in the mesenteric veins in man usually produces less severe results than ligation. It does not obstruct as quickly and therefore time is left for the development of sufficient collaterals. Hemorrhagic infarction is rare, and occurs only if all the smaller vessels have been occluded. There are many accidental causes which produce thrombosis and it occurs in all probability almost daily after operative interference. Thanks to the well developed collateral circulation and the slow formation

of thrombi, it is rare to find extensive injury, especially gangrene of the intestines (about 50 cases have been described).

The question of safety after ligation of small vessels in the intestines awakened general interest when gastric and intestinal resections were first performed. Madelung and later Rydiger (173) performed experiments on this question. They found it impossible to establish general rules as to which vessels of the mesentery of the small intestine could be ligated without danger of gangrene. As is well known, the mesenteric vessels branch into the so-called arcades. Individual arcades or annular anastomoses occur in varying number in the small intestines—about three to five. Individual arcades can, of course, be ligated, but the closer the ligature is applied to the intestine, the greater the danger, since the anastomoses become fewer as that region is approached. The attempt to determine metrically at what distance from the bowel the ligation would be devoid of danger, has failed completely, since the individual differences are too great. In injuries, however, as is easily understood, tears in the mesentery parallel to the intestines are always more dangerous than those that correspond to the radius of the mesentery.

The vascular supply of the large intestine is somewhat different; the arcades are fewer, and there is really a so-called marginal vessel running parallel with the bowel and sending supply branches into that organ. In this case, also, the results of injury may easily be deduced from the anatomical facts.

The microscopical findings in hemorrhagic infarction of the intestines have frequently been studied. It is very important that the injury should first affect the sensitive mucosa, which then becomes ulcerated. After ligation of one of the main branches of the mesenteric artery, the nutrition of the capillaries in the mesentery is also impaired and blood can pass through the vessel walls into the tissues, *i.e.*, by diapedesis. Even if ligation, injury, embolism or thrombosis, do not lead to an extensive gangrene, there may arise conditions of the intestines which indicate disturbances in nutrition. Most important are the ulcers, which are frequent, probably because of the greater sensitiveness of the mucosa. As the experiments of Schloffer (174) have shown, stenosis may occur from such ulceration, and possibly without it, and we find it occasionally as a cause of ileus. Physiologically, therefore, the most important factor in such cases is always the defective blood supply. When, therefore, a stenosis is discovered years after a crushing injury, it should not be assumed that the intestinal wall itself was injured directly by squeezing, but that the mesenteric vessels were involved, and as a result, a small amount of intestine became gangrenous. Busse (175) takes the same view in relation to tuberculous stricture of the intestines. He believes, on the basis of



pathological anatomical investigations, that, in such cases, the ulceration itself is not the cause of stenosis, but the injury to the blood vessel supplying the diseased area leads to a stricture, similar to those described by Schloffer.

The symptoms, following obstruction of the mesenteric vessels, depend on the intestinal infarction. Embolism and thrombosis cannot very well be differentiated in their symptomatology, even though their etiology is entirely different. Cardiac disease or arteriosclerosis must first be considered as causes of embolism, in which also a thrombus may form secondarily and involve the veins. In true mesenteric vein thrombosis, a thrombosis primary in the portal vein which secondarily involves the mesenteric vessels may be differentiated from a primary mesenteric thrombosis, but both are rare occurrences.

In view of the many injuries which occur to veins during operation, it is really remarkable that thrombosis is not observed more often. Small ones, as were studied by Payr (176), actually occur, but as a rule, they remain localized and produce very few, if any, clinical symptoms. It is only in intestinal obstruction that thrombi carried from the intestines, are important. An event observed, not rarely, is increasing infarction in a loop of intestine apparently healthy as it is released from a strangulated hernia. As is easily understood, this is due to the greater arterial inflow from the margin through the anastomoses, and simultaneous occlusion of the venous outflow (see above, under "retrograde incarceration"), the arterial supply having previously been interrupted because of separation or kinking and beginning again after liberation of the constriction. This progression of the nutritional disturbances in strangulated hernias is well known, and the practical deduction follows, not to resect too little, but from five to seven times more than the loop which was contained in the hernial sac.

Less surgical interest is attached to the much discussed "phlebosclerosis," *i.e.*, primary disease of the walls of veins with which thrombosis is associated. Furthermore, changes in the coagulability of the blood are also factors favoring mesenteric thrombosis, as the increased coagulability found by Schmorl (177) in eclampsia. It may be mentioned, in passing, that obstruction of the mesenteric vessels with the formation of aneurysms is not an unusual cause of death in horses infested with worms.

Of all the thrombotic processes in mesenteric vessels, those developing in connection with infections in the viscera are the most interesting in surgery. In these forms of thrombophlebitis, it is not the intestinal infarction which interests us, but the suppurative process in the veins, clinically characterized by pyemia, with chills and rigor, and which leads to multiple abscesses of the liver. We find this condition following gastro-

intestinal inflammations and ulcerations, cholelithiasis, occasional infections such as anthrax (178), and especially appendicitis (lit. see Sprengel (179)). If pus once enters the veins, a fatal outcome is almost certain, but Wilms (180) succeeded in saving a number of such patients by ligating the veins in the meso-colon. Late thrombosis may also occur following appendicitis (181), but strangely enough, it is quite rare in typhoid fever and dysentery (182).

Clinically, the severe pain in mesenteric embolism and thrombosis (183), which we have already mentioned in discussing abdominal pain in general, is very striking; blood appears in the stools from the ulcerative processes, and there is a rapid pulse as in all affections of the peritoneum. The latter should probably be considered a result of reflexes.

### PERITONITIS

One of the most important symptoms of peritonitis is the reflex rigidity of the abdominal walls, to which Trendelenburg especially called attention in the diagnosis of intraabdominal injuries (184). A. Hoffmann (185) has studied the conditions under which this rigidity appears by injecting irritant substances into dogs and goats—oil of turpentine proved to be most effective—first into the musculature of the abdominal wall, then into the muscles and nerves adjacent to the vertebral column, then into the exposed intercostal nerves and finally into the peritoneal cavity. By a suitable operative procedure, he was able to separate the parietal and visceral peritoneum. These experiments were intelligently combined with section of the sensory roots in the spinal canal, and finally, as a supplementary procedure, the irritants were also injected into the pleural cavities. As a result, he found that rigidity of the abdominal walls is a reflex process running by way of the intercostal and lumbo-sacral nerves. It is produced only when the parietal peritoneum is irritated, but may be easily produced through direct action on the intercostal and lumbo-sacral nerves, as occurs, for example, in kidney injuries, when there is inflammation in the region of the spine. These experiments explain the frequent observation that abscesses lying centrally in the abdominal cavity are not often accompanied by rigidity.

As has been mentioned above, appendicitis in its early stage is almost always accompanied by a peritonitis, probably toxic, and this fact explains the generalized rigidity. This sign, however, soon subsides, only to reappear when the appendix perforates and a purulent peritonitis is initiated. The inexperienced are therefore tempted in the beginning stage of an appendicitis to make a larger incision than is necessary. Irritation of the sensory nerves at their point of exit may also produce rigidity and thus

lead to diagnostic errors. Many a case of gun shot wound of the kidney or of perinephric abscess has been subjected to laparotomy because the abdominal rigidity suggested peritonitis or injury to a viscus, and in the literature, cases have been described of crushing wounds of the vertebral column in which this symptom was present to a high degree (186). Further, the experiments of Hoffman give an explanation for it, when it is present in pleuritis and pneumonia, for the abdominal muscles became very tense after the injection of oil of turpentine into the pleural cavity. The surgeon, now and again, sees cases of pneumonia diagnosed as appendicitis. But whether this is an "irradiation" as Hoffmann calls it, or whether it is actually an inflammatory process spreading through direct lymphatic channels (187), from the pleura to the region of the appendix, is not yet clearly determined.

Since abdominal rigidity is a reflex process, it follows that it occurs in irritations of the parietal peritoneum as long as the short reflex arc is intact, *i.e.*, it will occur even after section of the spinal cord in the middle or upper thoracic regions. This fact may also have occasional practical significance.

The most important disease of the peritoneum is acute bacterial inflammation (188). In the great majority of cases the primary cause lies in one of the viscera, the appendix, gall bladder, stomach or female genitalia (see in those chapters); in a small number of cases, the primary focus cannot be demonstrated. Corresponding to the great variety of intestinal flora, varied organisms are found in the exudate of peritonitis, and they are not only of one type, but a mixture of many varieties. It has been attempted, of course, to separate from the mixture a specific organism on which to lay the blame for the peritonitis, and on the basis of such investigations, for example in appendicitis, the colon bacillus has often been considered the offending cause. The fact, however, that a certain organism outgrows all others in the culture tube does not necessarily indicate that this particular bacterium is the cause of the disease. Indeed, every one with even a small amount of experience in bacteriology, knows that the colon bacillus grows especially easily and abundantly, and that it is impossible, or at least very difficult, to isolate other organisms from a mixture in a test tube in which this organism is implanted. We should only consider a bacterium the cause of a peritonitis in cases where it can be demonstrated that the body has developed antibodies toward it, such as agglutinins, etc. The work on animals which has attempted to establish the pathogenicity of an organism has also a certain value in peritonitis; all others are interesting only as illustrative contributions.

In the compilation of Weil (189), it is found that in the peritonitis following appendicitis, colon bacilli were present in 60 per cent. of the cases, *B. coli* and streptococci in 19 per cent. *B. coli* and other bacteria 4 per cent.,

streptococci in 9 per cent., diplococci in 3.5 per cent., and staphylococci in 1 per cent., the remainder was divided among *B. proteus*, *fecalis alkali-genes*, *pyocyaneus* and mixed infections without *B. coli*. The anerobes were not considered in these figures.

But it is just these latter which, according to newer investigations, are of particular importance in the etiology of gangrenous peritonitis (Veillon and Zuber, Tavel-Lanz, Ali Krogins, Friedrich, Heyde (190). There are, of course, different opinions concerning the classification of these anerobic organisms, but Heyde found *Bac. fusiformis*, *fragilis*, *ramosus* and anerobic staphylococci in his investigations. All of these types are highly toxic (toxin formers), and in fact, many of the cases of post-appendiceal peritonitis show the picture of a severe intoxication and not an actual sepsis. The anerobes just mentioned are putrefactive bacteria, hence the penetrating stench of appendiceal pus. Rumberg (191) found the agglutinin titer of the blood markedly increased to certain of these organisms, which fact is of interest for reasons above mentioned, even though it should not be overestimated.

In a large percentage of his cases of appendicitis, Heile (192) found an anerobic, spore bearing bacillus, probably belonging to the group of potato organisms, which had, like other anerobes, marked necrotising and toxic properties. In severe cases, the agglutinin titer was very high for these spore bearers, but unfortunately it was not determined in these investigations whether it was also increased for other bacteria.

For the etiology of post-appendiceal peritonitis, the recognition of the importance of these putrefactive organisms is a big step forward, for the frequent gangrene of the appendix was not readily explainable from our knowledge of those inflammations in which the ordinary pyogenic organisms were involved. How far the course of a peritonitis is influenced by such putrefactive organisms has not been revealed in detail, but clinically, it is not unusual to see very severe cases of post-appendiceal peritonitis in which the picture of a severe toxemia is developed. It has been attempted to differentiate streptococcus peritonitides from the others (193) but not without opposition. The agglutinin titer and the opsonic index have, thus far, not been found increased to streptococci (Runneberg), so that proof that these particular organisms are the decisive factors in the respective cases, is not complete.

A "chronic" peritonitis may be produced by mechanical irritation without infection, as shown by Wegner who repeatedly blew air into the abdominal cavity, and by Wieland (194) who introduced sterile foreign bodies.

This leads to the question of how bacteria gain entrance to the peritoneal cavity. In the first place, they may enter from the intestinal



canal through perforations, not only of the appendix, but also from the stomach or any other part of the intestinal tract, as for example, in typhoid fever; and the following rule has been enunciated: "the higher in the intestine the perforation, the more often are streptococci found in the pus; and the lower the perforation, the more frequently are colon bacilli present." It may be mentioned that, according to Cushing and Livingood (195), the bacterial flora in the upper gastrointestinal tract is less in variety and amount than that lower down.

The mode of infection of the peritoneum in perforations is not difficult to understand, and this is also true in gall bladder and biliary duct infections, and those of the female genitalia. Of course, it must not be forgotten that the peritoneum very stubbornly resists suppurative processes developing in its vicinity, and as shown in the experiments and clinical investigations of Meisel, it succumbs only when there is in addition a profound disturbance of its circulation (196). Ordinarily, pus pushes the peritoneum ahead of it, or stretches it. We are indeed justified in seeing an important protective mechanism in this elasticity and displacement of the peritoneum, as when we observe the serosa of the gall bladder stretched to two or three times its original size by an empyema of that organ.

It follows that in wounds through the abdominal walls in which there are no intestinal injuries, there is no great danger of infection, as numerous experiences in the war have shown (see Schmieden (197)). The experiments of Friedrich (198) show that the incubation time of peritoneal infections is about the same as in external wounds, namely from six to eight hours. In perforations of the stomach, much depends on whether it was caused by ulcer or carcinoma. As Brunner (199) found in animals, gastric contents, free of hydrochloric acid, as we often see it in carcinoma, are much more dangerous than the normal contents.

The cases of peritonitis in which no communication between the lumen of the organs and the peritoneal cavity can be discovered, are far more difficult to explain (200). The question of whether there is actually a penetration of the intact intestinal wall by bacteria has been examined experimentally from all viewpoints. Many workers attempted to find bacteria on the serosa or in the fluid, in incarceration of the intestines, especially incarcerated hernias. Their results do not harmonize entirely, but the differences may be explained by technical errors which need not be discussed. To summarize, bacteria were demonstrated only occasionally, and it was necessary that the intestinal wall be rather severely injured before they appeared in the serous fluid in hernial sacs. Ordinarily, the organisms normally present in the intestine do not penetrate its walls, as is taught by our every day experience (201).

The more important experiments are probably those which have attempted to show whether foreign organisms, pathogenic to the individual, would pass through the intestinal walls, when swallowed. This work also led to varying results, but it seems that virulent organisms can pass through an undamaged intestinal wall under certain circumstances, and lead to a general infection (202). The first researches on this question were undertaken by Kocher (203), but his results are not of value, because he produced injuries to the legs of his animals at the same time. Karlinkski (204) added staphylococci to the milk of new born animals and found a general infection in a goodly percentage of the cases. Of course, the objection that the portal of entry may not have been the intestinal tract, but the tonsils, for instance, cannot be gainsaid. Neisser and Buchbinder (205) could not convince themselves that the intestinal wall was permeable to bacteria, but both of these writers have paid too little attention to the virulence of their organisms. Clinical and autopsy observations of peritonitis arising probably from penetration through a diseased intestinal mucosa have been contributed by Langemaak, Lennander and Nystrom, Erkes and others (206). Penetration may also occur in the enteritis of children (Escherich, Baginski).

Among the peritonitides of unknown portal of entry, that due to the pneumococcus is of the greatest interest to surgeons (207). Jensen (208) could show in two guinea pigs, that feeding with virulent pneumococci gave rise to a fibrinous peritonitis; histologically, he found the intestinal wall loaded with organisms, although no ulcerations were present in the mucosa. Since pneumococcic peritonitis usually begins with diarrhea, Jensen believes it not improbable that the infection arises within the lumen of the intestine. This view, however, does not explain the fact that in the great majority of cases this disease occurs in girls. It therefore seems more logical to believe that the portal of entry is the genital tract. But clinically, nothing points to these organs, and at autopsy the tubes, ovaries, etc. are usually normal. But, minute histological examinations on the question do not seem to have been made. The studies of Krogius (209), Jensen and others show that the pneumococcus which is, of course, frequently present in sputum, is also found very often in the intestinal tract (for example, in appendicitis).

In adults, furthermore, pneumococcus peritonitis occurs with equal frequency in males (Jensen, author's observation). An extension of a pneumococcus infection from the lungs to the peritoneum, of which, indeed, it is tempting to think, is scarcely ever observed, although after injury to the pleural endothelium, bacteria may pass through the diaphragm. In animals, also, it is most difficult to obtain a peritonitis from an infection of the pleura (210), for according to Jensen, the current of

fluids is directed from the abdominal cavity to the pleura and not in the reverse direction.

The work of Peiser (211) especially, is directed toward the possibility of infection of serous surfaces, particularly the peritoneum, through the blood stream. "The serous membranes as long as they are uninjured, are impermeable to bacteria circulating in the blood stream." Invasion takes place only "in the moribund stage of a severe septic process when the bacteria at the height of their multiplication enter all the organs." If the peritoneum has been subjected to the action of even a mild irritant (physiological saline is sufficient), bacteria will enter the peritoneum very quickly. Whether they multiply, *i.e.*, whether a diffuse peritonitis results, depends on the virulence of the bacteria and the resistance of the individual. The same results were obtained in the pleura. The appearance of a peritonitis in sepsis is, therefore, the beginning of the end, and operation in such a condition is useless.

In discussing the reaction of the peritoneum to these invaders, Wegner has shown that it can protect itself against a certain number of bacteria by making use of its absorptive powers (see above). Grawitz (212) indeed, on the basis of his experiments, believed that the resistance of the peritoneum against bacteria is very high. But Pawlowski (213) opposed this view, for he found that pathogenic staphylococci when introduced intraperitoneally, always produced a fatal peritonitis; but saprophytic organisms were harmless. In spite of this, Grawitz, and with him quite a number of other authors, among whom may be mentioned Tavel and Lanz (214), (201), continued to hold the view that "primary bacterial peritonitis never occurs because this membrane either easily absorbs organisms or is entirely invulnerable to them." They believed that the peritonitis which occurred quite uniformly, as, for example, after laparotomies in laboratory animals in the older days, developed because of extensive injury to the tissues. If this be true, those cases of Pawlowski in which peritonitis occurred after the experimental introduction of bacteria were really the results of a primary infection of the incision or of the stitches. Doubtless, this explanation of Pawlowski's results is far fetched, and Reichel's observation (215) that it depends to a large extent on the virulence of the injected organisms is entirely correct. Moreover Walthard (216) introduced staphylococci into the peritoneum of an animal after an operative procedure, and a general peritonitis began from the places where the serosa was injured, especially by drying, and if this latter was prevented, no peritonitis appeared. These experimental infections are favored by the presence of such good culture media as blood or ascitic fluid, an observation which corresponds very well with our clinical experiences. In suppurative peritonitis, no one factor can be considered

the most important; there is a combination of bacteria, enzymes, toxins, resistance of the tissues, etc.

Surgical experience has taught us first, that a progressive infection of the peritoneal cavity from the abdominal walls rarely occurs, but that its possibility must not be ignored. Therefore, the warning is enunciated not to drain the abdominal cavity through the hernial orifice in strangulated hernias because of the danger of secondary infection (217). Secondly, the peritoneum is not as susceptible to infection as was believed, always provided that it has not been injured severely by mechanical means. Thus, for example, in the operations not strictly aseptic, such as opening the gastrointestinal tract, unavoidable slips in technique are followed much more often by infections of the abdominal walls, than by peritonitis. The former are therefore more susceptible than the peritoneum (217) and for this reason, we drain the incision and not the peritoneal cavity. At present, it is impossible to decide whether there has been an injury previous to the inflammation in the so-called "spontaneous" types, for example, pneumococcus peritonitis, or whether there is an infection through an intact membrane. The diarrhea which has been described as a precursor of pneumococcus peritonitis might easily injure the serosa.

What is the nature of the course run by a peritonitis (218), (214)? Experiments have demonstrated that in the first few hours after their introduction into the peritoneum, the number of the bacteria diminishes. This is brought about first, by absorption, second, by accumulation on the walls of the cavity where they are partly free and partly enclosed in leucocytes or endothelial cells; and third, by phagocytic destruction. There is of course no object in assigning a special importance to any one or the other of these processes, as was formerly done to absorption, but Notzel (219) could show that animals did not succumb to 100 times the minimum lethal intravenous dose when the same organisms were given intraperitoneally. On the other hand, animals with peritoneal infection may be kept alive by preventing absorption through ligation of the thoracic duct even though this does not exclude the possibility that bacteria may be found for prolonged periods in the blood stream. Jensen (208) in his experiments on pneumococcus peritonitis at least could detect the organisms in the blood in four to five minutes after they were injected intraperitoneally, and they remained there during the entire course of the disease. He contradicts Bordet's claim (218) that bacteria enter the blood in peritonitis only during the agonal period. This question of bacteremia has been frequently discussed in such peritoneal diseases as appendicitis. It will be considered more fully under that topic, but it might be mentioned here that it often occurs in this condition (Canon (220)). But whether Jensen's opinion, as he expresses it, "the decisive struggle



in peritonitis takes place not in the peritoneum, but in the circulation," is correct, depends somewhat on the viewpoint.

Peiser's (221) experiments show that absorption of bacteria from the peritoneum takes place in quantity, only in the first stages of the disease, later, absorption is much slower. Even in the cases with all the symptoms of peritoneal sepsis, absorption becomes limited, and the increase of the bacteria occurs rather in the blood. The fact that the peritoneum absorbs substances quickly only at first—as Peiser found in his sodium chloride solution experiments—and later, but slowly, to keep pace with the kidneys as it were, is a protection for the body against overwhelming amounts of bacteria and toxins. If this equilibrium is disturbed by the introduction of saline solution into the peritoneum, the animals die a septic death from increased absorption, while the controls remain alive. In operative cases, it was also occasionally found that death occurred very quickly if the peritoneum was irrigated, so that the impression could not be avoided that this procedure caused direct damage. But whether the injury occurs in the sense of Peiser, or whether in spite of careful technic, it occurs because protective adhesions are freed, is difficult to decide in a given case.

But now the parietal peritoneum on account of its smaller surface and poorer vascular supply absorbs much less than the visceral layer. To this difference Meisel (196) assigns the chief reason for the localization of secondary abscesses in peritonitis. In fact, these abscesses occur mostly in the peripheries of the abdominal cavity, that is subphrenic, in the lumbar region, in Douglas's cul de sac and in the hollow of the sacrum on the right side. Obviously the position of the abscess depends even more on the position of the organ in which the infection arose. The preference for the right side is related of course to the appendix. But delayed absorption on the part of the parietal peritoneum is probably also a factor which should not be underrated.

Another protective mechanism of the peritoneum is the leucocytes and their ability to destroy organisms. The fundamental studies of peritoneal phagocytosis were made by Metchnikoff (222), on the normal peritoneum, using not bacteria but the red corpuscles of the goose as objects for phagocytosis. Clairmont and Haberer (223) studying the subject under pathological conditions, found in guinea pigs that every exposure of the intestines, either moistened or dry, led to a leucocytosis which was greater than that produced by the injection of geese erythrocytes into the closed peritoneum. Phagocytosis by these leucocytes was very energetic at first but soon ceased, so that in later hours, when that in the control animals was at maximum, it had become almost zero in the operated animals. According to Metchnikoff (222) there is an increased

phagocytosis in the exudate of peritonitis. The morphology of the process has been studied particularly in relation to bacteria, and it has been found that the mononuclear form of leucocyte, which is normally present in the peritoneal cavity, is the first cell to engulf the invader. After phagocytosis, the leucocytes perish (Metschnikoff (224)), or they deposit themselves on the peritoneum. After this period of mononuclear leucocytosis there is a period of leucocytic diminution, which, however, lasts but a short time. In a few hours after the injection, polymorphonuclear forms appear in great abundance, and these now take up the struggle. At first large numbers of bacteria are engulfed, but this phagocytosis soon ceases, and if the pus is examined in the following period, there are found but few bacteria enclosed within leucocytes. They seem to undergo some unknown change which make them unpalatable, but freshly added bacteria, especially if they are of another kind are easily phagocytosed (225). This period of diminishing phagocytosis does not continue until the death of the animal, but usually increases shortly before, with simultaneous disintegration of the leucocytes. Wallgren therefore believes that substances are set free from the destroyed leucocytes which rupture the protecting shell of the bacteria and thus render them again susceptible to the phagocytic process.

This is not the only method by which the abdominal cavity is protected. The peritoneal fluid under normal conditions has bactericidal properties and this faculty of clumping and dissolving bacteria is increased by the presence of leucocytes, which on destruction—perhaps also because of a secretion—liberate antibodies into the surrounding fluid (226), (202). But not only the leucocytes, but the endothelial cells also produce such agglutinins, precipitins and bacteriolysins.

As a prophylactic measure after an operation, when a general peritonitis is feared, attempts to produce a leucocytosis in the peritoneal cavity are made so that antibodies will be brought to the situation where they will be needed. This has been done particularly in gynecological procedures on the day before operation by the injection of nucleic acid or camphorated oil (227). Perhaps delayed absorption after the latter substance has been injected also helps. Just as this artificial procedure awakens the protective powers, so do the spontaneous suppurative processes stimulate the peritoneum to reaction. According to Moskowicz (228), even in the earliest stages of appendicitis, there is diffuse irritation of the peritoneum which produces a relative immunization of that membrane. If the disease progresses, this previous immunization will possibly prevent or at least hinder the immediate involvement of the entire peritoneum. This is said to explain the relatively quick and efficient localization in appendicitis and the surgeon practices the rule of not inter-

fering too much with the adhesions in appendiceal abscesses, but knows that draining the abscess cavity alone is sufficient (179). This irritation of the entire peritoneum is caused, according to Hagler (cited by Sprengel), by the entrance of toxins. It is also possible in animals to protect against further infection from the peritoneum by previously injecting cholera organisms in small numbers (229).

Investigations to discover whether the exudate itself has antibacterial properties were undertaken by Pansini, R. Stern, R. Pfeifer, Schrader (230) and others. Apparently it has none; at least, in Schrader's experiments, bacteria grew in the exudate, though not as well as in bouillon. It seems however, to possess an inhibiting influence on intestinal organisms, but the statements of various writers on this point do not agree entirely.

It has already been mentioned that the tendency of the peritoneum to form adhesions and to localize infections is another very important protective mechanism.

If the bacteria are highly virulent, they develop, notwithstanding all the natural protections. If the infection is mild, and does not lead to a fatal issue, the whole course of the disease is slower. Leucocytes begin to accumulate only after a few hours have elapsed, and are never so abundant as in the severe types. The mononuclears predominate in these milder forms and they are also usually in the majority at the end of a peritonitis. The bacteria are often not given the opportunity to multiply, but are phagocytosed in a few hours. Between these two extremes there are all gradations, but the struggle for supremacy always proceeds in the same way.

Unfortunately it is impossible to give a prognosis of the disease from the type of organism found in the exudate. Even the discovery of streptococci is not necessarily decisive; such organisms not rarely produce a peritonitis which runs a very benign course. We have treated several cases in which the cause could not be definitely determined, but in which streptococcic pus flowed from the abdominal cavity. The patients recovered, although in the further course, several abscesses formed and were evacuated. But these organisms, and as far as I know other cases in the literature, have not been examined for their hemolytic power.

Furthermore, the severity of the clinical course and the degree of pathological anatomical change do not always run parallel. We often see only a slight congestion of the serosa, with scarcely any exudate, except a few flakes of fibrin, in cases which have run a very severe course. The term "septic" has been applied to this type, not a well chosen word, because according to our present knowledge, every patient with peritonitis is more or less septic.

This leads us to a discussion of the cause of death in peritonitis. An exhaustive review of the older literature is given by Heinecke (231) who has also performed extensive experiments on this problem. According to the majority of writers, an intoxication is the cause of death, to which factor may be added a sort of shock, not clear, however, in its details or action (232). Heinecke sectioned the small intestines of rabbits and determined the blood pressure by the same methods which Romberg and Passler used in the investigation of diphtheria and other infectious diseases. The animals died about 12 hours after operation, and Heinecke could demonstrate that the circulatory disturbance in the peritonitis from perforation is due to a paralysis of the vasomotor center in the medulla oblongata. Damage to the heart is certainly done in the early stage of collapse, but in the later stages, heart action is impaired principally because of an insufficient supply of blood resulting from the vasomotor paralysis. Respiratory disturbances appear later than those of the circulation, but respiratory failure precedes cardiac failure. Both may probably be considered due to central paralysis of the medulla oblongata, and, according to Heinecke, this results from the direct action of bacterial products, and not reflexly through transmission by the nervous system.

Friedlander (233) has submitted these investigations and conclusions to a rather interesting criticism. He believes it necessary to separate the rapidly progressing sepsis as it occurred in the researches of Heinecke and Romberg from the slowly progressing actual peritonitis. On account of the fact that the pulse rate and temperature are not proportional, he believes that reflex influence cannot be entirely ignored. He produced a "peritoneal irritation" in animals by ligation or removal of the omentum, and then found that the pulse rate was proportional to the temperature if the vagi were cut; if they were intact, the pulse rate was higher. Strehl (234) could not confirm these results in intestinal obstruction in rabbits and cats, and found that there was no difference in the pulse rate when the vagi were sectioned at the cardia. Extirpation of the celiac plexus also had no effect on the pulse rate in peritonitis. But even if Friedlander's experiments could not be verified, at least one of his ideas is valuable, namely, that peritonitis is not merely a sepsis with quantitative differences, but that, in the death from this disease, the complicated nervous supply of the abdominal cavity must also be taken into consideration. Whether such influences on the circulation and respiration are demonstrable, remains for future experiments to decide. Braun and Boruttau, and Perthes (235) also found the blood pressure remained normal for a long time, and it showed a tendency to fall suddenly, only shortly before death. Careful blood pressure determinations in peritonitis have also been made by Lichtenberg (236).



Paralysis of the intestines must also be considered in the causes of death from peritonitis, and Askanazy (237) believes the dilatation of lymphatic channels around the ganglion cells in the intestinal walls is the anatomical basis of the paralysis. This explanation is doubted by Walbaum (238), but the anatomical finding has been confirmed by Strehl on cat's intestines which were quickly placed in fixative while still living. According to the prevailing opinion, this intestinal paresis is of toxic origin. The resulting distention of the abdomen and absorption of decomposing intestinal contents, act as injurious and finally destructive factors on the entire body. But this general opinion, as it is usually taught, is probably incorrect; at any rate Hotz (98) has shown experimentally, that the intestine, the serosa of which shows peritonitis but no distention, will give practically the same motility tracing as the normal bowel. Paralysis, therefore, is not demonstrable. For the same reason, the statements that meteorism and intestinal paralysis are consequences of inflammation of the coeliac ganglion, have thus far not been proved. The distended intestine has, however, an entirely different form of movement and the question in this case is: What is the cause of the distention?

The researches of Enderlen and Hotz (18) have shown that, as in fully developed ileus, there is a markedly diminished absorption from the intestine in peritonitis, and in the later stages, there is actually an outpouring of fluid into the intestinal lumen. The works of Clairmont and Ranzi and of Braun and Borrutau (239) also lead to this conclusion. There is, consequently, in peritonitis, the same close relation between distention, paralysis and circulatory disturbance that we have studied in ileus. At operation in early peritonitis, markedly contracted and markedly dilated segments are often seen side by side. Whether this is due to an unequal distribution of the injury to the circulation or not, still remains in doubt.

A symptom of intestinal paralysis in the late stages of peritonitis is vomiting. This terminal fecal vomiting must be differentiated from the vomiting and singultus at the beginning of peritonitis, just as it must be done in ileus. In appendicitis, we often observe these symptoms in the very beginning, but, as Sprengel (240) points out, they disappear again when an abscess has been encapsulated. Vomiting is very rare during the stage of formation of the abscess, but it reappears when rupture takes place, and a diffuse peritonitis sets in. It is the irritation to the peritoneum which causes vomiting, and this is present, as stated above, in the earliest stages of every appendicitis. This type must, therefore, be considered reflex through stimulation of the vomiting center by way of sympathetic fibres. More details are given in the pages devoted to gastric motility. Since this vomiting is purely reflex, it is easily understood that it occurs more readily in some individuals, and in others, not

at all. According to Nothnagel (112, p. 530) singultus does not necessarily mean that the peritoneal surface of the diaphragm has been affected, since the phrenic nerve sends branches to other regions of the peritoneum.

As stated, the reflex vomiting in the early stage of a peritonitis must be differentiated from the fecal vomiting in the late stages. The character of this latter is entirely different from the reflex type. The descriptive term "running over" has been aptly used to describe it (241) on account of the quantity and the absence of associated abdominal compression. The fecal odor, however, is not evidence that it comes from lower levels, *i.e.*, large intestine. Decomposition takes place in the small intestine, where, on account of paresis, certain bacteria are given free rein (Nothnagel). If the paralyzed intestine now becomes filled with more and more feces and fluid, then according to the theory of Hagenot in 1713 (241) the abdominal compression forces the contents toward the stomach, and it is emptied in the direction of least resistance. The question of whether antiperistalsis which has been discussed in detail on previous pages, plays a part has caused much controversy. This type of movement cannot be of much importance in fecal vomiting which occurs, as stated, only after the intestinal muscle is paralyzed, and when it no longer reacts to stimuli. With this theory of Hagenot, it is necessary to assume, furthermore, that the pylorus remains open; an assumption thus far not proved, and which really contradicts that which we otherwise know of the act of vomiting.

Like all the other general symptoms of peritonitis, vomiting has also been considered due to an "intestinal intoxication." This question has been discussed more in detail under ileus where the conditions are clearer. In all probability we may safely conclude from the investigative results recounted that "intoxication" is not very important, first, because the intestinal contents are not so poisonous in fecal stasis, and second, absorption is diminished in peritonitis and ileus (18). Moreover, vomiting is not observed after the experimental injection of stagnant intestinal contents (239). Finally, it must not be overlooked in considering Hagenot's theory, which ignores the vomiting center altogether, that it is not entirely clear why certain animals, *e.g.*, rabbits, do not vomit at all after being subjected to the same mechanical conditions in the experimental production of an ileus.

Occasionally, although only in a very small percentage of the cases, hematemesis occurs in peritonitis. This has been called "vomito negro," as in yellow fever. The theories concerning gastric hemorrhage have been discussed under gastric ulcer and parenchymatous gastric hemorrhage, and these sections may be consulted for details. Doubtless, the infection plays a very important part in the hematemesis of peritonitis, at least, it is usually found only in the most severely septic cases.

In the treatment of acute peritonitis, the question of *drainage* is encountered in addition to the primary evacuation of the pus.

In the literature a distinction is not always made between tamponade and drainage, probably because of the idea that the tampon, *i.e.*, the strip of gauze, would also help in evacuating the fluids. This was combated by Chrobak and Volcker (242) who pointed out that the meshes of the gauze are quickly filled by the thick flowing viscid mass, and thus it is changed to a practically solid body. The experiments with solutions of dyes cannot be compared to the conditions in patients (see (243)). A wick acts better in drawing off, if care is taken to prevent compression by the edges of the wound. In the experiments of Rotter (244) such a wick led off in the first seven hours as much fluid, and probably more, than a drain. But as we shall presently show, after twelve hours, no more pus finds exit even through a rubber tube introduced into the abdominal cavity, so that there is no difference in this respect to a strip. If a strip is packed too tightly into a wound, or if it is compressed by sutures in the abdominal wall, it acts only as a "tampon," *i.e.*, like a cork, and does not drain.

For these reasons, a drainage tube is used if it is desired to evacuate pus, and tampons are used if hemorrhage cannot be controlled, or if it is advisable to stimulate adhesions, *e.g.*, to help in the encapsulation of an abscess. The foreign body is such an effective stimulus to the formation of adhesions that a pus focus will be walled off from the remainder of the abdominal cavity in twelve hours (Volcker). It is easy to understand that a tampon may occasionally be used to close a fistula or fill up an empty space (Volcker). Now these adhesions which develop so quickly around a strip of gauze, no matter how well the technic is carried out, make it impossible to drain the entire peritoneal cavity. Indeed, even such a mild irritant as a rubber or glass tube stimulates the formation of enough adhesions to prevent the evacuation of pus except from the sinus through which the drain passes. If there are other abscesses, they may not be influenced at all by the original drainage. A recognition of these principles in surgery and gynecology was acquired quite early, but broad drainage usually accompanied by tamponade, was combated at first, and then later, drainage in ordinary so-called aseptic or half septic abdominal operations. Even today, there is a divided opinion on drainage in peritonitis (245).

But the point accepted by all is that the whole abdominal cavity cannot be drained in this disease; it is only a question of whether it is possible and advantageous to drain those regions, which experience has taught us are sites where abscesses localize. Rehn and his school (246) are of the opinion that during and after peritonitis, the pus tends to collect almost exclusively in Douglas's cul de sac, therefore after irrigation, they



place a drainage tube there and lead it through the operative incision; *e.g.*, in appendicitis this would be to the right, at the level of the spine of the ileum. Otherwise, the abdomen is firmly closed and Rehn believes that the pus is forced out by the viscera which sink downward toward the pelvis in conformity to the laws of communicating tubes. This opinion has aroused opposition, particularly from Rotter (244) who has investigated the subject both experimentally and at the bedside. He placed a loop of intestine in a vessel containing water and found that one half of the loop sank, which was natural since its specific gravity is one, and that the water rose in the drain, which may be considered as a lateral leveling tube, only as high as its level in the vessel. There was no sign of a forcing out of the fluid through this tube. It can take place only when the fluid is under a certain tension, which may occur in peritonitis as long as the intestines are markedly distended or when a gas containing abscess is formed in a space firmly closed by solidly adherent loops of bowel (Proping). That the exudate will be forced out through a drain in the cul de sac by the sinking of the intestines is, therefore, an erroneous idea. The law of communicating tubes cannot be evoked in the case of the abdominal cavity because bodies of different physical states are present (solids and liquids), one of which floats on the other. Rehn in his theory did not consider the "upward pressure." Furthermore, he assumes that all, or the greatest part of the exudate formed, flows continuously into the cul de sac. This assumption is also incorrect, as Rotter showed, because after twelve hours, almost nothing drains from the tube, and separation from the free abdominal cavity must have occurred. The fluid which reappears later comes probably from the granulations of the drainage tract. By forcing water into the canal under pressure, Rotter also showed that the drainage tract ceases to communicate with the free abdominal cavity, since all the water returned freely around the tube. But that all drainage should be considered illusory because the openings in the tubes occasionally become plugged with omentum or intestines, is also incorrect.

If the operation in peritonitis is confined to simple incision without irrigation, nothing at all flows from the drain in the cul de sac, because the amount of pus is not sufficient. That which is evacuated in the first twelve hours in cases treated by Rehn's method, is chiefly the water from the irrigation, which Rotter advises removing by dry sponging. After mopping, Rotter closes the abdominal cavity tightly, provided that the cause of the suppuration is removed and no necrotic bits or other sequestra remain. This is an extremely important point; the abdomen is not closed completely if, for example, the appendix had been covered and enmeshed in dense adhesions. The clinical results by this procedure are said by Rotter to be equally as good as those treated by drainage (Rehn's method; see also



(247)). English and American authors, many of whom had already closed the abdomen before Rotter, have reported very good results by this method (248). Nevertheless, as Chrobak expresses it, "an active procedure always excites more favor than inactivity" and thus the closure of the abdominal cavity advocated by Rotter on such reasonable grounds, is followed by few surgeons. Douglas's cul de sac may be drained better through the vagina or rectum as Friedrich (190), Bordenheuer (247), Wilms (248) and others have advised, than by Rehn's drainage. The latter method is, however, better than drainage through the lumbar region (Rotter). But none of these methods is effective for prolonged drainage because of reasons made clear above. The vaginal or rectal route has long been in use, of course, for the evacuation of secondary abscesses.

By *chronic peritonitis* is meant a process which does not begin with suppuration, but one in which the anatomical picture is dominated by "thickenings and adhesions of inflammatory origin" (112). Naturally, the etiology of this disease will be varied, even though tuberculosis is a frequent cause of these diffuse inflammatory conditions. In those of local nature, a slowly progressing appendicitis, salpingitis, diverticulitis, etc. and organisms similar to those producing acute inflammations will come under consideration. The type is not difficult to understand, and is of great importance in the causation of ileus. But the question of whether such chronic adhesive forms of peritonitis arise without previous bacterial inflammation, has not as yet been solved. We have found through the many laparotomies that are performed daily, that a "pericolitis" is by no means rare. It has been described by Rokitansky and a number of French and English writers. Virchow (249) was familiar with it, and in addition to those in individuals with a "rheumatic tendency," he believed it resulted from trauma and diseases of "intraabdominal channels." Today we cannot add to this excellent definition. The meaning of "trauma" in the widest sense of the word, may be studied daily in laparotomies. And it was these observations, especially in patients who had been operated several times, that showed the special tendency of certain individuals to the formation of adhesions (250). The cause of this "connective tissue energy" is unknown (251). But that certain humans and animals respond more readily than others with connective tissue formation, under the same stimulus, is proved by clinical observation and animal experimentation. When Virchow speaks of a "rheumatic peritonitis," this statement only shows that he occasionally found extensive adhesions without adequate reason in the history and the findings. If we speak at present of "predisposition" it shows only that we observe these things from an altered viewpoint. Unfortunately our actual

knowledge of the reason why one organism shows a greater tendency to form adhesions than another has not been increased since Virchow. Although an individual may form connective tissue with the greatest readiness, nevertheless, some external stimulus which causes this formation must always be present, and thus in chronic adhesive peritonitis the question arises, is this stimulant bacterial or not? We know very little regarding this. Bittorf (252) has observed true primary pericolitis in conjunction with pneumonia. In such cases it is, of course, perfectly natural to think of bacterial infection, either a slight general peritonitis or a spread of the infection through the lymphatics, as assumed by Franke (187). According to Virchow, the most frequent cause is constipation, an opinion which is generally accepted even today (Rosenheim (253), Bittorf, Payr). But it must never be overlooked in these cases that pericolic adhesions are also very frequently the cause of constipation and not its result (254). It is not clear how constipation causes pericolitis, but from the experiments mentioned above, it might be assumed that bacteria wander through the congested intestinal walls, although according to our experience to date, this only occurs with very virulent bacteria, and then rarely. It is also not known whether toxins penetrate the intestinal wall in constipation. Both conceptions are possible, but nothing is proved. Actual fecal stasis is by no means the rule in constipation (see section on constipation), and the pericolitis may only be the consequence of purely mechanical irritation. As stated above, Wieland could demonstrate its development experimentally after mechanical stimulation. At any rate, further investigations, especially bacteriologic, are necessary in this problem.

The consequences of chronic peritonitis, and its resulting adhesions, can be seen in the mechanical interference with defecation (255).

We shall deal later with the formation of bands, and the ileus caused by them; but will speak of the two places in the intestines at which more serious difficulties arise from diffuse adhesions, *i.e.*, at the junction of the ileum and the cecum, and at the splenic flexure. Payr has performed exhaustive work on this latter form of chronic stenosis of the colon. Gas blocking may be caused by such surface adhesions about the splenic flexure, and with the distention by gas the same discomfort is caused as in colonic ileus, *i.e.*, periodic severe pain with every contraction of the gas filled segment. Even normally, the splenic flexure is a difficult spot for the passage of contents (23); it is so firmly fixed by the phrenico-colic ligament to the diaphragm and to the abdominal wall, that an acute angle forms in the concavity of which the intestinal wall lies as a fold. It is possibly due to this angular kinking of the splenic flexure that, as Roith states, feces are usually found in the ascending and transverse colon in

the cadaver, while the descending colon is, as a rule, empty. That fluids and feces can pass through this narrow region more easily than gas, has been shown by Quenu, who caused water to pass easily under only  $\frac{1}{2}$  m. pressure even with the most pronounced kinking to an acute angle. Therefore the stenoses described may justly be considered gas-blocking, *e.g.*, as it is frequently seen in our irrigator tubing.

Polyserositis occupies a special position among the forms of chronic peritonitis. We understand thereby a disease which manifests itself suddenly with ascites or peritoneal irritation, then it runs a gradually ensuing chronic course which points to congestion in the regions drained by the portal vein. This congestion in the portal circulation can be caused by a narrowing of the inferior cava in the pericardium (Pick's pseudo-cirrhosis of the liver) or by occlusion of branches of the portal vein within the liver due to perihepatitis (Zuckergusleber). The actual acute stage of the inflammation of the serous membranes, which affects the pericardium in addition to the peritoneum, has probably no uniform etiology; it seems that all types of infection may be causes. The second stage of portal vein congestion is of greater surgical interest. In addition to frequent paracentesis, the other operations discussed under ascites have been tried, including decapsulation of the liver. As far as I know, the pericardial adhesions in this disease have been left alone; but Rehn (257) has performed a splitting of the sternum in juvenile adhesive pericarditis with supposedly good results.

Of all ulcerative diseases of the bowel, *appendicitis* or epityphlitis is of the greatest surgical interest, since it is the disease which is the most frequent cause of acute diffuse peritonitis. Without doubt, the physiological importance of the appendix is not especially great, at least no ill consequences which might seem to have arisen from its absence have been observed following the numerous appendectomies. Comparative anatomy shows that an appendix is present in anthropoid apes, in lemurs, and in the opossum, as well as in man (258). The dog also has an appendix well differentiated from the cecum.

The abundance of lymphoid tissue in the appendix is anatomically most remarkable; and it is reasonable to suppose that this lymphoid tissue has a certain functional importance in the economy of the organism (259). A protein splitting and a carbohydrate splitting enzyme have been found in the appendices of fistula dogs (260), and it is demonstrable that the intravenous injection of appendiceal secretion causes active peristalsis in the intestinal tract of the rabbit (261). But we know that all intestinal juice shows a similar action, and great caution is necessary to avoid erroneous deductions regarding the importance of this particular intestinal secretion. Furthermore, Heile could trace certain relations of the

appendix to the ileocolic muscle which is situated at the valve of Bauhin, insofar as a meso-appendicitis, or novococain injections, led to a relaxation of the sphincter. It is advisable to be cautious in evaluating these findings also, since it is naturally conceivable that the sphincter itself becomes affected by this injection or inflammation. At any rate, it has not as yet been proved that removal of the appendix or its mesentery causes insufficiency of the ileocolic muscle.

Now the inflammations of the appendix show anatomically a fairly uniform picture (262). According to the undivided opinion of all authors, the first change, *i.e.*, that due to a slight attack which may be easily repaired, is a lesion of the epithelium in the appendiceal crypts, and in its place we find a membrane consisting of leucocytes and fibrin. If the inflammation progresses, the epithelial defect enlarges, the whole appendiceal wall thickens and becomes infiltrated with pus, thus forming a true phlegmon. This condition, which can be reached even in the first 24 hours, may also regress, but it generally leaves a narrowing of the lumen which favors a new attack, as we shall see presently. The third stage is characterized by progressive destruction of the wall, either from penetration of the superficial mucosal ulcers, or from rupture of the abscesses. This leads to perforation, peri-appendicitis, and finally peritonitis, with all the reactions of the serosa as described above.

It is remarkable how these anatomical changes may be repaired. It always produces astonishment when an appendix is removed about one-fourth year after a large abscess has been opened.

The question arises, what are the conditions under which this anatomical picture develops? What causes this destruction of the wall from within outward? In the first place, it must be remembered that infection is one of the most essential factors in appendicitis, but this factor must not be overemphasized. It has been shown by numerous investigations (263), (190), (193), (191), that colon bacilli, streptococci, staphylococci, pneumococci, influenza bacilli and many other organisms, including numerous anaerobes, may be the sole or predominant organisms. But a specific organism for appendicitis does not exist, nor can deductions be drawn from the bacteriological findings as to the course of an appendicitis. Although Haim claims that he has seen an especially malignant form from the streptococcus, there are so many contradictory observations on record that this statement has no general application. It is to be remarked that many authors found in the peritoneal exudate in appendicitis, bacteria differing from those normally in the intestine (191). Nevertheless, according to our pathological physiological conceptions, it is impossible that the organisms found should be the only causative factors in this disease. It would indeed be most peculiar if such bacteria should only



show a predilection for the appendix and ignore the other portions of the intestines, with the possible exception of the diverticuli (Meckel's, sigmoid flexure). All things considered, we are forced to the conclusion that an important factor is the appendix itself, *i.e.*, its anatomical singularity.

First of all we must discover how bacteria enter the wall of the appendix. Obviously, this may take place either through the blood or from the lumen of the organ. Certain clinical considerations, *i.e.*, the sudden attack, the rapid destruction of the wall, the early general involvement of the whole body, as seen, for example, in the increase of leucocytes, etc., suggest an hematogenous infection, but in the later stages there is not always anatomical pathological uniformity. In many organs, *e.g.*, kidney, parotid gland, prostate, an inflammation in the sense of an excretory inflammation has been demonstrated, which means epithelial destruction without demonstrable change in the blood vessels, from direct hematogenous infection. This fact naturally has theoretical importance in relation to appendicitis. Kretz (264), for instance, believes that his findings in a number of severe and quickly fatal cases point to embolism as the causative factor, but this interpretation has been assailed. Attempts have been made to decide the source of infection by experimental means (265), (263). The results show in the first place, that it is possible to obtain embolic foci with inflammation and necrosis of the wall, by intravenous injection of almost any bacteria, although those are best which had been grown from spontaneous appendicitis in animals of the same type. But embolism was found also in other organs. Secondly, experimental appendicitis can be evolved from the mucosa, if steps are taken to occlude the lumen against the cecum as may be easily done by the introduction of a foreign body (paraffin, etc.). Ligation with silk thread gave variable results.

But these experiments do not satisfactorily decide the question in point. Both groups of investigations have only this practical interest for the surgeon, they prove that the appendix can be destroyed either by hematogenous infection, or by infection direct from the bowel. The route must be decided in each case by a combination of clinical observations and pathological anatomical investigations. This method will show us that cases such as were reported by Kretz, *i.e.*, severe embolic destruction of the appendix, are really rarities, and when irregular circumscribed perforating ulcers of the size of a lentil, are seen in cases with sudden onset, they are probably of embolic origin. But in the majority of cases, the infection comes most likely from the bowel, and as stated, the possibility is deducible from the anatomical structure of the appendix. Being a terminal organ it empties itself of feces which enter it, in spite of the valve of Gerlach, with more difficulty than any other intestinal segment (266).

To this must be added that its position is often very unsuitable for discharging its contents, *e.g.*, it may be retrocolic, or kinked by adhesions, or by position changes of other organs, as the cecum. In the appendices of adults the emptying is made still more difficult because former slight inflammations have left scars which narrow the lumen. At least, these scars found so frequently, are considered to have this etiology at present, while formerly there was a tendency to conclude from them that the human appendix was an organ showing retrogressive changes. This difficulty in discharging its contents causes a more marked decomposition of the feces ("vas clos" after Dieulafoy (445)), not in the sense of a bacterial increase, but on the contrary, the number of bacteria decreases as shown both in humans and animals, but, according to Heile, probably more in the sense of increased toxicity of its contents. Experiments of Klecki (268), Dieulafoy (240), Hartmann and Mignot (240) have shown that the virulence of the bacteria increases if the appendix is closed, or the wall is injured by ligation of vessels (Klecki) and their toxins supposedly destroy the mucosa.

It is quite plain that the weakest point of the enterogenous theory lies here, if it depended solely on bacteria, it is difficult to understand why other intestinal segments, *e.g.*, the cecum, should be immune from such destructive infection. For this reason, it is impossible to completely ignore the condition of the appendiceal vascularization if we wish to abide by this theory. This has been recognized by many (269) and a number of mechanical factors which may influence its blood supply have been sought. Klauber (270) is of the opinion that displacements and strangulations of the mesoappendix cause nutritive disturbances, and that, therefore, the conditions are similar to those in strangulated ileus. Other authors believe that tension of the walls caused at first by catarrhal swelling of the mucosa, or from inflammatory hydrops behind an occluding fecal concretion, will produce deficiency in the appendiceal blood supply. But we must bear in mind that appendicitis is rare in catarrhal enteritis, and nursing babies who develop catarrh of the bowel in its purest form, very rarely develop appendicitis. Fecal concretions have also been held responsible for compression of blood vessels, but probably erroneously, because it is certain that gangrene of the wall does not always begin where the fecal concretion is located but rather directly distal from this place. Atrophy of the mucosa as a possible consequence of the pressure of a fecal calculus, has been frequently described. It is often claimed that the concretion is an inflammatory product, but this is difficult to prove. Since animal experiments, described above, have shown that appendicitis can only be obtained if the lumen is closed, and since in man the inflammatory process is observed remarkably often distal to a fecal concretion occluding the

lumen, or from a scar narrowing it, it seems quite justifiable to assume a certain causative relation between the occlusion of the lumen and the appearance of the inflammation in the sense spoken of above. The fact that the most destructive cases of appendicitis usually show a fecal concretion (Sprengel), can also be very easily interpreted that the calculus is formed of cast-off mucosal cells.

But according to Brunn (271), the blood supply may also be affected by a spasm in the fine capillaries which supply the mucosa and this may be induced by bacterial toxins. The conditions would be quite similar to those in gastric ulcer. Brunn, in order to support this very tempting viewpoint, searched for relations between vascular distribution and inflammatory changes, and actually found that gangrene always begins where one of the vertical side branches springing from a main branch, enters the wall of the appendix. His microscopical findings emphasize the importance of the vascular supply. In appendicitis there always exists a combination of "inflammatory stasis, and hemorrhagic infarction" in the vessels, *i.e.*, the same process as found in gangrene of a loop of small intestine. If the interruption of the vascular supply in the small intestine is of but short duration we first find, as stated above, nutritional disturbances in the mucosa. It is only when this interruption is prolonged that the other coats also become necrotic. The process is probably similar in the appendix. The ultimate cause of this supposed vessel spasm is unknown, but it might be due to increased toxicity of contents produced by partial or complete closure of the appendix, and possibly the nutrition also plays a certain role (see below). This view is naturally hypothetical, and many details must still be investigated both experimentally and clinically, especially as regard the vasoconstricting effect of confined intestinal contents, but the doubts which made it difficult to consider appendicitis an enterogenous infection from the clinical view point, have largely been dissipated.

There is a strong belief, that diet and general habits of living are the causes of the frequent appearance of appendicitis.

And indeed it is remarkable, as McLean (272) points out, that in certain peoples, especially the Chinese, appendicitis is practically unknown, while Germans or Englishmen living there are affected as frequently as at home. As a matter of fact, appendicitis has undoubtedly increased in the last few decades, even if erroneous diagnoses are considered. But whether nutritional factors are at fault is difficult to say. It has also frequently been stated that appendicitis became more rare during the war, and this was supposedly due to vegetarian food. But it must not be overlooked that before the war, appendicitis was very frequent in a section of the population which did not eat meat to excess (Germany).

For the present, all these hypotheses must be accepted with caution, and can not be verified by impressions, but only by statistics. An example of one of these can be presented thus: according to Aschoff, appendicitis is quite frequent in young folks of our civilization but is relatively absent in people living closer to nature because the intestines of the latter children are more resistant, having longer natural nutrition. But this is also merely a vague hypothesis.

Perhaps our whole viewpoint in appendicitis is too much confined to the local process. Just as we show a tendency today to consider peptic ulcer more and more as a symptom of a general disease, Hoenck (273) has attempted to build up a similar theory for appendicitis. Little is gained by his observations inasmuch as the diagnosis has not been confirmed by operative evidence in even one case. But on the other hand, it has been justly pointed out (Sprengel 240, p. 209) that removal of the appendix in the early stages of inflammation certainly puts an end to the disease, forcing upon us again and again, the conception that it is a local condition.

Above all, the invariable increase of leucocytes, points to a general reaction of the body, and while this leucocytosis and the shifting of Arneth's blood picture is considered by Sonnenburg (274) an answer of the body to peritoneal irritation, he nevertheless observes that leucocytosis also appears in closed appendiceal empyema, *i.e.*, without peritoneal involvement. Furthermore, in other forms of peritonitis, *e.g.*, pyosalpinx, the leucocytosis is not so marked, which proves that it cannot be considered as the simple consequence of peritoneal irritation.

Some of the clinical symptoms deserve short discussion. Kafemann (275) has described in detail the pain sensations in his own case of perforating appendicitis. At first the patient complains of pain of varying intensity over the entire abdomen, especially in the epigastrium; perforation is described as "the sudden plunging of a saw tooth knife into the abdomen, and the repeated twisting of the weapon within the belly." The explanation of this pain must be practically similar to that in "indigestion and peritonitis" as described above. Thus the diffuse pain at the beginning of the disease is due probably to the presence of free peritoneal exudate. It is a common observation, noticed in other diseases also, that abdominal pain is frequently localized in a place distant from the seat of trouble, especially in the epigastrium. It is usually assumed that at the beginning of peritonitis, there is increased intestinal motility and this is responsible for localized pain (Wilms). But there is much uncertainty, and the reason why abdominal pain should always be epigastric, has not been found. The pain in the right side of the lower abdomen is probably due simply to irritation of the parietal peritoneum, but



Sonnenburg (274, p. 102) believes that "appendicular colic" is produced by the attempts of the appendix to expel its contents. The extent of involvement of the regional nerves or lymph vessels is uncertain in the well known sensitiveness to pressure at McBurney's point. This pain on the right side is also seen in pneumonia and one of these two routes must surely be affected. On the basis of his anatomical investigations, Franke (187) thinks that it is due to continuation of the inflammatory process via the lymphatics. But it is not quite so easy to explain why there should be such severe pain at the moment of perforation, for the peritoneum, which is destroyed during perforation, is the visceral layer which is supposed to be insensitive. We must assume that the escape of even minute quantities of air, feces, etc., are sufficient to exert a very severe irritative effect on the parietal peritoneum. But it is still very remarkable that perforation of the stomach or appendix should produce such severe pain at the moment of its occurrence, while traumatic ruptures or stab wounds are not necessarily painful, at least, not at first. The only assumption that can be made is that the preceding inflammation has made the peritoneum especially sensitive. It is still an open question whether vascular changes also are involved in producing these pains (276).

As a further evidence of the above statement, that even a slight appendicitis can not be explained from the view point of a local process alone, is the fact that such patients are quite sick from the very beginning. Kafemann, like most patients, thus describes it: "In the evening, perfectly well, only to wake up in the morning with marked sensation of illness." Until further knowledge, we must consider the impairment of general well being, which is usually more acute than in other intestinal conditions, as a septic or toxic process, although as stated, a bacterial examination of the blood is usually negative. The presence of albumen in the urine is probably also of toxic origin; likewise icterus, which, however, is rarely seen.

It must be remembered, furthermore, that in the later stages of appendicitis, there is often infection of the retroperitoneal tissue in addition to that of the peritoneum. This explains occasional differences in the usual course of peritonitis, *e.g.*, the often dangerous "septic" process with its rigors and pulmonary emboli (Sonnenburg 274, p. 130). All these symptoms point to the fact that in appendicitis the essential factor is not bacterial invasion of the wall of the appendix, but the defense, successful or otherwise, which the body sets up throughout the infection. If appendicitis were only a local disease there should be more similarity to gangrene of the bowel, as, *e.g.*, in strangulated hernia.

Another question, very complicated, and thus far not generally solved is this: Why are some forms of appendicitis so malignant, while others

are readily encapsulated? There is no special tendency for encapsulation in the appendicitis of youthful individuals; on the contrary, we quite frequently see the very severe forms of peritonitis in children. The other ordinary factors must of course count, as bacterial virulence, bodily resistance, extent of necrosis, etc., but the details of the conditions are not quite clear.

It is, moreover, rather difficult to find an acceptable explanation of why appendiceal abscesses which are not opened by operation, show a tendency to rupture through the abdominal wall, *i.e.*, actually through the thickest part of the abscess wall, and less frequently into the bowel. This is probably due, in the first place, to anatomical conditions, as a retrocecal position of the appendix, etc., but also to the fact, as pointed out by Sprengel, that the abdominal wall forms the side of the abscess which is least able to yield to pressure, while the intestines are more free to move. It must further be considered if nutritional conditions also are involved, they are certainly better in the intestinal wall than in the wall of the abdominal cavity. Altogether, however, this problem is by no means solved.

Chronic appendicitis, so called, merits special discussion and as a disease conception has acquired an especially great importance in French literature (274), (240). Doubtless very different things are understood by the name of chronic appendicitis, and careful differentiation and separation are necessary to obtain insight into the question. If we begin with the anatomical picture, we know of certain appendiceal changes not related to an acute attack, but which present a cicatrizing process in the widest sense of the word. To this class belong appendiceal obliterations and adhesions to surrounding organs, including the changes in the blood vessels which are described in detail by v. Redwitz (276). The congenital anomalies in position are, of course, not included here.

Whether obliterative appendicitis is an involution process or is the result of chronic or acute inflammation has been discussed for a long time (277). But so far as a decision from anatomical evidence is possible, the investigations of Miloslavich and Namba (278) have demonstrated that in young individuals it is due chiefly to inflammation, while in older persons, sclerosis of the submucous and mesenteric arteries might also be responsible. That these latter changes can be inflammatory also, has been shown by the investigations of v. Redwitz. Therefore the anatomical changes may be caused by some form of a slow chronic process or by acute attack. In the former it is proper to speak of "chronic" appendicitis. In the second case these changes are only the end result of an acute attack, and the disturbances should be regarded as due to adhesions and pulling, or to inflammatory vascular and nerve changes.

The therapeutic results in chronic appendicitis show that differentiation of the otherwise similar anatomical findings, according to the clinical viewpoint, is entirely justified. Because, as the reinvestigations of Melchior and Loser have shown, in the operations of those cases in the second group, *i.e.*, the so-called "interval operations," 94 per cent. of the patients are cured, while in all such cases not preceded by acute appendicitis, only 60 per cent. of cures are effected by removal of the appendix. Furthermore, operative results in group one are satisfactory only if actual gross changes are found in the appendix. Aschoff (279) and others believe that all appendiceal changes are due to a former acute inflammation and not to a chronic process. It must, however, be stated that cases are known in which this form of pathological anatomical change is found, without a history of any previous acute attacks (pressure atrophy of the mucosa from fecal concretion (280)). This must suffice for the present, although it can not be denied that light attacks may have been overlooked. Since the anatomical picture only shows conditions as they are, it is impossible to state from it alone, whether the changes observed actually demonstrate a previous attack.

Thus far, we are on fairly secure ground. v. Redwitz sees in vascular injury the reason for the attacks of pain induced by chronic appendicitis. They resemble arteriosclerotic changes very markedly and therefore, like these, can produce colicky pain.

But especially in the French literature, a chronic appendicitis is recognized even if the changes in the appendix are so minute that, according to our conception, with due regard to the pathological anatomical viewpoint, we can not find in them a sufficient explanation for the subjective suffering. Cases are known to every surgeon in which a diagnosis of "chronic appendicitis" is made on account of illy defined abdominal pain, and an appendectomy is performed. These are probably included in the above mentioned tabulation given by Melchior and Loser with about 60 per cent. of cures. The fact that appendectomy gave no relief in 40 per cent. of the cases shows that the appendix was not the only cause of the trouble.

But conversely, cases are also known and frequently reported in the literature, in which recovery followed, even though the pain did not implicate the appendix alone, but gastric and general abdominal pains, etc. were also present. This brings up the question: is there any known relation of the appendix to other organs, in the sense that discomforts localized in other organs are actually incited by changes in the appendix itself? Such relations have frequently been assumed. Payr (281) states that gastric fissures and ulcerations are due to emboli resulting from chronic appendicitis, and Moynihan (282) also emphasizes that the symp-

toms of chronic appendicitis can resemble most markedly those of gastric or duodenal ulcer and even hematemesis may be observed. Hyper- and hypochlorhydria, "dyspepsia," etc., have been frequently described (283). French authors speak of an hepatic form of chronic appendicitis (284) accompanied at times by icterus, and believe there are toxic and infectious factors at work. Renal, vesical and pulmonary disturbances, the latter partly masked as asthma or tuberculosis, are cured by appendectomy (284). Even a symptom complex called "pseudotuberculosis" has been created. It is not quite just to refute all these descriptions as errors of observation without more ado, although sometimes a little more critical examination seems desirable. But the final conclusion that the appendix should be the cause of all these different disturbances, seems erroneous. With these symptomatic differences, the disease of the appendix could either be only a part of a causative general disease which must yet be found (see gastric ulcer), or it is secondarily involved in other diseases, as was explained in constipation. Recovery, following the removal of the appendix, at any rate, does not prove that it was the cause of the disease, for it must be remembered, that with this operation and the after treatment, many possible factors are added which may lead to the disappearance of the symptoms.

In this symptom complex of chronic appendicitis, it is easy to distinguish those disturbances which have been described more in detail in the chapter on constipation, and which have their cause in affections of the colon, especially of the cecum (motile cecum, typhlatony, etc.). But that nonspecific acute inflammatory processes are occasionally observed in the cecum also, has been proven by the anatomical investigations of Jordan and Seck, and also by the reports of Fischl (285).

In *resections*, the length of intestine which must be removed depends, generally speaking, on the extent of the disease or injury and not on the actual free will of the operator. Nevertheless, the questions of how much can be removed, and what disturbances result, are of great interest, since they have considerably enlarged our knowledge of the physiological importance of the different parts of the intestine.

The most extensive intestinal resections carried out on man were done successfully by v. Brenner, 540 cm., Ghedim, 534 cm., Nigrisoli, 520 cm., Axhausen, 475 cm., Pauchet, 400 cm. (286). All these patients, to whom a large number of others might be added, stood the operation very well, and although they showed some nutritional disturbances at first of which we shall speak presently, they afterwards lived and ate like normal individuals. But nearly all died a short time afterwards, as Denk (287) discovered by inquiry, although only the patients of Brenner and Pauchet died from the actual intestinal disturbance; the others from intercurrent diseases and



also from recurrence of ulcers. It must be agreed with Denk, that the resistance of the patients is lowered by extensive intestinal resection. From the large number of published cases, an idea can be gained of the length of intestine which can be removed from an individual without directly jeopardizing his life. Since the length of the intestines varies in different individuals, as stated above, the ratio of the part removed to that of the part remaining must always be considered. These reports have shown that one-half and slightly more of the small intestine can be removed, without endangering life. If the removed part amounts to 80 per cent. or more, grave symptoms are observed practically always and death ensues. These numerical proportions in length are very similar in animals, especially in the dog.

The disturbances in metabolism and intestinal digestion which follow such extensive resections have been studied in numerous experiments and by observations on man. Trzebicki and Monari (288) made simple estimations of weight and found that seven-eighths of the small intestine could be resected without causing loss of weight, while after resection of eight-ninths to nine-tenths, although the animals remained alive, they lost one-third of their weight permanently.

In the extensive resections in humans, it was with few exceptions the ileum which was removed. Various authors have tried to determine whether resection of the jejunum is more dangerous. Trzebicki, Albu, and Blayney, believe, on the basis of their experiments, that removal of the jejunum is less well tolerated than that of the ileum, while according to the statements of Diliberti-Herbin (289), Takayasu, Soyesima, Monari a.o., no difference exists. With these opposed results, it may surely be said that the difference between the two resections can not be great. The investigators who emphasized the danger of jejunal resection assumed that this part of the intestine was an especially important region for the absorption of nutritive substances. This view is erroneous, because Lieblein's (290) studies have shown the absorptive power of two loops of equal length of jejunum and ileum to be equal (see also above under "absorption"); indeed in fat absorption, the ileum is even more important. London (291) found in fistula dogs, that the ileum absorbed abundant protein; and Sivre emphasizes this point particularly.

But large resections of the small intestine are procedures which always cause considerable disturbances of the digestive processes immediately after the operation. Diarrhea, loss of weight, sometimes bulemia and thirst, are the symptoms uniformly described, and it has already been mentioned that the intestine remains "sensitive" for a considerable time afterward. Nevertheless, a certain, even almost complete equilibrium is created, and the question of how it is brought about and which part of the

intestine establishes this balance in each case has been answered in the experiments of Stasoff (292) on fistula dogs. After resection of 164 cm. of ileum not only does an increased secretion of gastric juice occur, but gastric digestion lasts two hours longer than normally. Intestinal movements were slowed in the jejunum above the place of resection, cleavage of the chyme progressed further, and more was absorbed, so that only half of the chyme now appeared at the fistula which was situated close above the resection. In the following months this state of compensation failed and the animals died with diarrhea and general loss of strength. Therefore, according to these investigations, the stomach, duodenum and jejunum substitute for the resected ileum, while it was found in other experiments, where the colon was removed later, that this part of the intestine does not participate in these compensatory processes.

Conditions are different after jejunal resection. Stasoff removed 132 cm. of this portion of the intestine and found that the reflex causing the flow of bile excretion and pancreatic juice which is incited from the duodenal and jejunal mucosa, was not diminished by removal of the jejunum; on the contrary, more pancreatic juice was produced. It was shown by experiments in which one fistula was established in the duodenum, and a second just above the valve of Bauhin, that after jejunal resection, the chyme when it reaches the colon is less digested than before operation, and also that less protein, carbohydrates, and fats, are absorbed in the small intestine. The degree of protein digestion remains almost unchanged, but that of carbohydrates is diminished. Thus the colon must compensate for the resected jejunum, but as far as fats are concerned, the task is somewhat beyond its powers (288).

The alterations in the digestive activity, as shown in these fistula dogs, must affect the general metabolism, at least after those resections which are on the border line of the possible. Metabolism determinations have been made in large numbers on men and animals, and show, with considerable uniformity, that the utilization of carbohydrates is good, that of proteins, although sufficient, is much impaired, while fat utilization is the poorest of all (286), (287), (289), (293). From these findings, Lieblein has drawn very interesting practical deductions for the nutrition of such patients. Accordingly, to compensate for the insufficient absorption of proteins, abundant food rich in nitrogen must be supplied, and meat is the best, since animal nitrogen is more easily assimilated than vegetable nitrogen. It is inadvisable to increase the intake of fat for purely mechanical reasons, because excess of fat makes the action of the digestive juices on proteins more difficult and those fats which are easily absorbed, or what is the same, most easily liquefied, as olive oil, goose fat or lard,

must be preferred to those which liquefy with difficulty. Carbohydrates may be given abundantly, especially since they spare proteins (294).

The anatomical results of these compensatory processes were studied in animals by Monari, Nagano, Flint (295) and others, and hypertrophy and hyperplasia of the mucosa were found. But Trzebiecki, Evans and Brenizer (296) in animals, and Barker (297) and Denk in man, could not demonstrate any anatomical changes which might be considered due to the resection. For the present, these anatomical findings are quite uncertain.

*Prolapse of the rectum, i.e.,* protrusion of the rectal mucosa after every bowel movement, is a condition which has its origin in various anatomical and physiological factors. In about 70 per cent. of the cases children are affected, middle age is rarely touched, while in advanced age it again appears more frequently (298). The prognosis in children is favorable, less so in adults. From these facts, it must be concluded that an essential etiological factor is present in the condition of the tissues, *i.e.,* in their tonus. This increases in children, but in adults after a certain age limit, it decreases. This diminished tissue tonus and the relaxation of the pelvic floor is readily demonstrable in patients with rectal prolapse (299), and Ludloff (300) found microscopical degeneration of muscle fibres and hypertrophy of the connective tissue in this neighborhood. Only in very rare cases will it be possible to discover the reason for these changes. Without quoting single cases, Beresnegowsky (301) states that typhoid fever, repeated childbirth, etc. will cause such muscular weakness. Bell and Hirschberg (302) describe rectal prolapse after trauma. In both cases, the prolapsus and the primary muscle weakness developed possibly from hemorrhage into the spinal canal, *i.e.,* of central origin.

But how does a weakened pelvic floor lead to prolapse of the rectum? Pathologically anatomically, prolapsus of the mucosa must be differentiated from actual prolapse of the rectum. The latter is a true hernia. In the earliest stage, Douglas's cul de sac and its content of intestines, bulge into the anterior wall of the rectum, which does not necessarily extend to the outside. It is only gradually that this invaginated portion passes through the anal opening. The perineal part, *i.e.,* that part of the rectal mucosa which in the male begins at the prostate, and which is very closely attached to its surroundings, remains at first fixed in its position (prolapsus recti), but in a later stage this also becomes loose and everted and thus an "eversion fold" in its ordinary sense ceases to exist (prolapsus ani et recti). The modern conception of the pathogenesis of prolapse is based chiefly on the anatomical investigations of Waldeyer (303), and was further amplified by Ludloff, who also added clinical evidence. The older opinion, subscribed to by Esmarch (304), is that the prolapse of the perineal part is primary, and that only in the progress of the disease a

prolapsus of the other tissue layers of the rectum occurs. This opinion may still be correct in the prolapse of children, although systematic investigations are lacking. At any rate, a pure anal prolapse is more frequent in childhood. It is probably only accidental that Ludloff found but 3 cases in his compilation of 100 from the literature. True prolapse of the rectum, *i.e.*, where a true transition fold still remains, while the perineal part has not yet been everted, is without doubt, a rare occurrence (4 cases in 100 according to Ludloff).

But if we consider the classical prolapsus ani et recti, *i.e.*, the type which includes 87 per cent. of all such cases, the low level of Douglas's cul de sac must be considered the chief predisposing factor (305). We find from the investigations of Zuckerkandl and Trager that in children the cul de sac of Douglas is always lower than in adults. In the male it reaches to the upper margin of the seminal vesicles; in the new born, to the lower margin of the prostate; in children to the level at which the ureters enter the bladder. The investigations of Napalkow (301) and Beresnegowsky show that its low level is an absolute necessity for the development of a rectal prolapse. Experimentally, they produced a rectal prolapse on cadavers of children first by filling the pleura with plaster of Paris to fix the diaphragm, and then pumping formol solution into the abdominal cavity under a pressure of one-half to two atmospheres. After prolapsus was established, the bodies were hardened by intraarterial formol injection and freezing; and it was found that the floor of the peritoneal sac was always below the line which connects the coccyx with the lower border of the symphysis. As long as the floor of the pelvic peritoneum was not below this line, no prolapsus occurred. In all cases of prolapsus, the coccyx had assumed an almost vertical position, and this is a further very essential factor. Physiologically, the coccyx is always more vertical in children than in adults, and this change to the vertical position supposedly occurs in adults if prolapsus recti develops. But it is not quite clear whether we are dealing with a causative factor, or more probably with a sequel. Actually, the direction of the intraabdominal pressure is changed by the vertical position of the coccyx, for ordinarily it is directed against the sacral hollow, meeting its resistance in the bone (306). But if this hollow is absent, as it is in the vertical position of the coccyx, the rectum instead of presenting its concave surface from behind forward assumes a straight direction, and thus the pressure on the bowel, and on the soft parts of the pelvic floor, is undoubtedly increased. Mummery, with this point in mind, has advised that children who show a tendency to prolapse should attend to their stool with legs strongly adducted, he attempts by these means to direct intraabdominal pressure more strongly towards the sacrum.



Apart from the weakness of the pelvic musculature, it was also believed that ligamentary attachments of the rectum had become loose if prolapsus occurred. This relaxation was thought somewhat similar to that in sliding hernia. Jeannel (307), who advanced this theory, points out that with perineal rupture or section of the sphincter, no prolapsus occurs, while the strongest sphincter cannot prevent the protrusion of a loosened bowel. Jeannel uses a very effective simile when he says that the bowel is like a chained prisoner. 'The cell might be left open, but as long as the chain holds, the prisoner cannot escape. With the chain broken, the closed door might still prevent the flight of the prisoner but he would escape as soon as the door opens, and Verneull, in defence of this much assailed opinion of Jeannel, continues: "and the door opens during every bowel movement." Jeannel's opinion contains a kernel of truth, but its author presented it one-sidedly, and thus encountered considerable opposition (308). It cannot be denied that in consequence of his theory his advice to perform colopexy has been followed by good results. In animal experiments (Ludloff (300), p. 760), it has indeed been shown that a prolapsus does not continue in the dog even if the rectum has been loosened far enough that it can be pulled easily through the anus, provided that the musculature of the perineum and the sphincter is not injured. But these experiments prove little in opposition to the opinion of Jeannel; they only show how important a good perineal musculature is, and explain why attempts at improving its tonus should be made by massage.

The factors mentioned, namely, weakness of the pelvic muscles, low position of Douglas's cul de sac, vertical position of the coccyx, too loose fixation of the bowel, all favor the development of a prolapse, but they do not cause it. To these must be added the intraabdominal pressure which first invaginates Douglas's cul de sac, *i.e.*, the anterior wall of the rectum into the rectum, thus forming the perineal hernia. The greater this abdominal pressure and the oftener it operates, the easier it is for the rectum to be everted, and this explains why constipation favors a prolapse, exactly as it is favored by diarrhea and catarrh of the intestine.

Therapy has taken all these details into consideration, and there are a large number of methods for operative treatment. After all that has been said above, it is natural that no preference can be shown to one method, but that according to the various causes and favoring factors, often a combination of several treatments must be applied.

#### LITERATURE TO INTESTINES

1. Dreike: Deutsche Ztschft. f. Chir., 1895, V. 40, p. 43.
2. Beneke: Deutsche Med. Wochenscht., 1880.
3. Enderlen: Deutsche Zeitschft. f. Chir., 55, p. 419.

4. Esau: Bruns Beitrage, V. 60, p. 508.
5. Lit. see Babkin: "Die aussere Sekretion der Verdauungsdrusen," Verlag Springer, 1914.
6. Cohnheim: Zeitschft. f. physiol. Chemie, 1901, V. 33, p. 451.
7. Weinland: Zeitschft. f. Biol., 1898, V. 38 and 40.
8. Adolph Schmidt: Klink. d. Darmkrankheiten, Wiesbaden, 1912, V. 1, p. 33.
9. Scheponalnikow: Diss. St. Petersburg, 1899.
10. Glinski: Diss. St. Petersburg, 1891.
11. Molnar: Deutsche Med. Wochenschft., 1909.
12. Pflugers Arch., 1890, V. 46.
13. Reichel: Zentralbl. f. Chir., 1896 and Deutsche Zeitschft. f. Chir., 1893, V. 35.  
Justi: Mitt. a.d. Grenzgebieten, 1902, V. 10. Narath: Arch. f. klin. Chir., V. 52. Baracz: Zentralbl. f. Chir., 1894 and Arch. f. Klin. Chir., V. 58.
14. Fr. Miller: Virchows Arch., 1893, V. 131, Suppl.
15. Ad. Schmidt: Darmkrankheiten 1, p. 41, also more of composition of feces here.
16. Cohnheim: Virch. Arch. 1877, V. 69.
17. Hamburger: Arch. f. (Anat. u.) Physiol, 1896, p. 332.
18. Enderlen and Hotz: Mitt. a. den Grenzgebieten, 1911, V. 23.
19. Ury: Arch. f. Verdauungskrankheiten, 1909.
20. See Abderhalden: Lehrbuch d. physiol. Chemie, 2nd. Ed., 23.
21. Heile (Roehmann): Mitt. a. d. Grenzgebieten, 1905, V. 14.
22. Kaoru Omi: "more fluid and sugar is absorbed from the jejunum than the ileum,"  
Pflugers Arch. f. Physiol., 1909, V. 126. Frey: Pflugers Arch. f. Physiol., 1908, V. 123.
23. Roith: Anatomische Hefte, 1903, V. 20, p. 64-65.
24. Rost: Arch. f. klin. Chir., 1912, V. 98.
25. Stierlin: Ergebn. d. inneren Med., 1913, V. 10; Klinische Roentgendiagnostik d. Verdauungskanals, Wiesbaden, 1916, for further lit. Rieder: Fortschr. auf. d. Gebiete der Rontgenstrahlen, 1911, V. 18, p. 99. Schwarz: Munch. med. Wochenschft., 1911, p. 1489, 1624, 2060. Holzkecht: Munch. Med. Wochenschft., 1909, No. 47. Borchers and Klatsch: Zeitschft. f. exp. Pathol. u. Therapie, 1913, V. 12, p. 221-295; Deutsche med. Wochenschft., 1913, p. 1294. Elliot and Smith: Journ. of Physiol., 1904, V. 31, p. 272. Cannon: Am. Journ. of Physiol., 1902, V. 6, p. 251. Langley and Magnus: Journ. of Physiol., 1905, V. 33, p. 34. Magnus: Pflugers Arch., 1902, 1903, 1908, 1911. Bayliss and Starling: Journ. of Physiol., 1899, V. 24, p. 99 and 1901, V. 26, p. 125.
26. Starlin: Ergebn. d. Physiol., 1902, p. 455. Magnus: Ergebn. d. Physiol., 1908, V. 7, p. 41.
27. Grutznher: Pflugers Arch., 1898, V. 71, p. 492 und Deutsche med. Wochenschft., 1894, No. 48, u. 1899, No. 15.
28. Nothnagel: Handbuch, V. 17, p. 6.
29. Trendelenburg: Deutsche med. Wochenschft., 1917, p. 1225 and Arch. f. exp. Path. Pharm., 1917, 81, p. 55.
30. Albert Muller: Arch. f. d. ges. Physiol. V. 116 and Mitt. a.d. Grenzgebieten, 1911, V. 22.
31. David: Mitt. a.d. Grenzgebieten, 1919, V. 31.
32. Muhsam: Mitt. a.d. Grenzgebieten, V. 6, p. 451. Prutz and Ellinger: Arch. f. Klin. Chir., V. 67, p. 970 and V. 72, p. 415. Glassner: Wiener. klin. Wochenschft., 1904. Enderlen and Hess: Deutsche Zeitschft. f. Chir., 1901, V. 59, p. 240.

33. Bose and Heyrovsky: Arch. f. klin. Chir., 1909, V. 90, p. 587.
34. Raiser: Inaug. Diss. Giessen, 1895.
35. Bayliss and Starling: Journ. of Physiol., 1900-1901, V. 26, p. 107.
36. Bloch: Med. Klin., 1911 and Fortschr. auf d. Gebiete der Roentgenstrahlen, 17.  
Boehm: Fortschr. a.d. Gebiete d. Roentgenstrahlen, 8 u. 18. Stierlin Rieder:  
Deutsche Zeitschft. f. Chirurgie, V. 106; Zeitschft. f. klin. Med., 70; Munch. Med.  
Wochenshft., 1910 u. 1911.
37. cf. Boehm: Arch. f. exp. Pathologie and Pharmak., 1913, V. 72.
38. Elliot: Journ. of Physiol., 1904, V. 31, p. 159.
39. Katz and Winkler: Beitrage z. exp. Pathol., 1902, p. 85.
40. Grodel: Fortsch. r. d. Gebiete d. Roentgenstrahlen, 1913, V. 20, p. 162. Dietleu:  
Fortschr. a.d. Gebiete der Roentgenstrahlen, 1914, V. 21, p. 23.
41. Genersich: Progr. medic., 21. Dauriac: Progr. medic., 21.
42. Blauel: Brun's Beitrage z. klin. Chir., 1910, V. 68.
43. O. Krauss and Henle: Arch. f. klin. Chir., V. 44, p. 410.
44. Toldt: Sitzungsher. d. Kais. akad. Wissensch. Wien, 1894, V. 103, 3, Div.
45. v. Bergmann and Lenz: Deutsche Med. Wochenshft., 1911, p. 1425.
46. Strauss: Therapeutic Monatshefte, 1906, p. 373.
47. v. Frankl-Hochwart-Frohlich: Pflugers Arch., 1900, V. 81, p. 455.
48. Goltz and Ewald: Pflugers Arch., 1896, V. 63, p. 381.
49. Matti: Deutsche Zeitschft. f. Chir., V. 101.
50. Goltz: Pflugers Arch., 1874, V. 8, 479.
51. L. R. Muller: Deutsche Zeitschft. f. Nervenheilkunde, V. 21, p. 86.
52. see Cohnheim: Nagels Handbuch f. Physiol., V. 2, p. 642.
53. Roussi and Rossi: Compt. rend. Soc. Biol., 1908, V. 64, p. 604.
54. Merzbacher: Pflugers Arch., 1902, V. 92.
55. Lit. see Schmidt: Darmkrankheiten, 1912; Strassburger im Handbuch d. inneren  
Medicin, V. 3, 2 part.
56. Stierlin: Munch. Med. Wochenshft, 1910, No. 27. Meyer-Betz and Gebhardt:  
Munch. med. Wochenschrift, 1912, No. 2, 33-34.
57. Ury: Arch. f. Verdauungskrankheiten, 1908, V. 14, p. 506.
58. Ad. Schmidt and Strassburger: Arch. f. Klin. Med., 1901, V. 69, p. 570.
59. R. Schutz: Arch. f. Klin. Med., 1908, V. 94. Oppler: Deutsche med. Wochen-  
schft., 1896, No. 32. Einhorn: Arch. f. Verdauungskrankheiten, 1896 u. 1898,  
V. 1 u. 3.
60. Schittenhelm and Weichardt: Deutsche med. Wochenshft, 1911, No. 19.
61. see Kaufmann: Spez. pathol. anatomie, 3, Edit., p. 439.
62. Riedel: Chirurgenkongress, 1912, p. 256; Deutsche Ztschft. f. Chir. V. 67, p. 422.
63. Anschutz: Naturforscherversammlung Breslau, 1904.
64. Muller: Chirurgenkongress, 1912.
65. Hertz: Constipation and allied intestinal disorders, London, 1909, p. 118.
66. Straup: Therap. Monatshefte, 1906, p. 373.
67. Gant: Constip. and Intest. Obstruc., London, 1910.
68. Groedel and Seybert: Ztschft. f. Roentgenkunde, V. 13, 4 to 5.
69. S. Perthes: Arch. f. klin. Chir., 77. Konjetzny: Brun's Beitrage, 1911, V. 73.
70. Hertz, Axtel: cited in Chir. Kongr. Zentralbl., 1913, 3, p. 595.
71. Pennington: J. A. M. A., 1900, V. 35, p. 1520. Gant: Krankheiten d. Mast-  
darms u. Afters. Deutsch von Rose.
72. Goebel: Med. Klink., 1910, p. 1771.
73. Rost: Mitt. a. den Grenzgebieten, 1915, V. 28.

74. Hartmann and Quenn: Chirurgie des Rectums, 1897, Paris.
75. Rossolimo: Neurolog. Zentralbl., 1891, p. 557.
76. Albu: Berliner Klin. Wochenscht., 1907, p. 1649.
77. L. R. Muller: (destruct. of lumbar spinal cord means constipat.), Zeitscht. f. Nervenheilkunde, 1901, V. 21, p. 86.
78. Stiller Glenard: Die asthenische Konstitutionskrankheit, 1907, Stuttgart.
79. Pinkus: v. Volkmanns Sammlung klin. Vortrage, 474-475.
80. Ebstein: "Die chronische Stoolverstopfung Stuttgart, 1901, p. 18.
81. Sturtz und Sauerbruch: Munch. med. Wochenscht., 1913, V. 60, p. 625.
82. Stierlin: Deutsche Ztscht. f. Chir., V. 102, p. 426 and ergebn. d. inn. Med., 1913, 10, p. 471.
82. Wilms: Verh. d. Deutsch. Ges. f. Chir., 1911.
83. Boehm: Munch. med. Wochenscht., 1912; Deutsches Arch. f. klin. Med., 1911, V. 102 and Arch. f. exp. Pathol. and Pharmak., 72, p. 1.
84. Stierlin: Klin. Roentgendiagnostik d. Verdauungskanales, 1916.
85. Boas: Med. Klinik., 1908, p. 1685 and Arch. f. Verdauungskrankheiten, V. 15. Mathieu: Arch. de maladie de l'app. digest., 1908, No. 11. Pflanz: Prager med. Wochenscht., 1908, No. 50. Fleiner: Berl. Klin. Wochenscht., 1893, p. 60. Albu-Kretschmer: Med. Klinik., 1908, No. 52.
86. Schwarz: Munchner. med. Wochenscht., 1911, No. 28 and 1912. Holz knecht and Singer: Munch. Med. Wochenscht., 1911, No. 48 and Deutsche med. Wochenscht., 1912. Singer: Die atonische and spast. Obstipat. in Albus Sammlung etc. in V. 1, No. 6; Wien. kl. Wochenscht., 1909.
87. Rost: Deutsche Zeitscht. f. Chir., 1919, V. 151.
88. V. Redwitz: Deutsche med. Wochenscht., 1919, p. 931.
89. Jackson's and other ligaments of the proximal colon: Arch. des. med. de l'app. dig., 1913, V. 7. Rjesanoff: Chirurgia, 1913, V. 33, p. 326.
90. Eastmann: J. A. M. A., 1913, V. 61, Discussion.
91. Schlesinger: Deutsche med. Wochenschrift, 1918, V. 37, p. 515.
92. Schmidt und Lohrich: Deutsches Arch. f. Klin. Med., 1903, V. 79, p. 383.
93. Fischler: Munch. med. Wochenscht., 1911.
94. Nothnagel: Lit. and discussion, Nothnagels Spec. Pathol., V. 17, p. 180; Wilms: Der Ileus in Deutsche Chir.; Leichtenstein in Ziemssens Handb., V. 7, 2 part.
95. Leichtenstein: v. Ziemssens Handbuch d. spez. Path. V. 7.
96. Zoge von Manteuffel: Arch. f. Klin. Chir., 1892, V. 41. v. Wahl: Arch. f. Klin. Chir., V. 38 and Zentralbl. f. Chir., 1889.
97. Kader: Deutsche Ztscht. f. Chir., 1891, V. 33.
98. Hotz: Mitt. a.d. Grenzgebieten, 1909, 20.
99. Zuntz and Jacke: Deutsche med. Wochenscht., 1884, p. 717 and Tacke: Inaug.-Diss. Berlin, 1884.
100. Kocher: Mitt. a.d. Grenzgebieten, 1899, V. 4.
101. Talma: Ztscht. f. Klin. Med., 1890, V. 17.
102. Trousseau: cited Deutsche Med. Wochenscht., 1884, p. 717.
103. Heineke: Arch. f. klin. Chirurgie, V. 83.
104. Olshausen: Ztscht. f. Geburtshilfe and Gynak., V. 14.
105. Ranke: cited by Albert, Lehrbuch d. Chir., 1882, V. 3, p. 234, 2nd Ed.
106. Wilms: Rupture, Deutsche med. Wochenscht., 1903, p. 81, u. 369; Arch. f. klin. Chir., 1913, V. 69.
107. Kertecz: Deutsche med. Wochenscht., 1903, No. 23 and Berlin. klin. Wochenscht., 1904, No. 52.



108. Kocher: Deutsche Ztschft. f. Chir., 1877, V. 8. Lossen: Arch. f. Klin. Chir., 1874-1876, V. 17 u. Bd. 19. Busch: Arch. f. Klin. Chir., 1875, V. 19. Roser: Zentralbl. f. Chir., 1875, 1886, 1888, Arch. f. Heilkunde, 1864. Further lit. Schmidt: Unterleibsbrüche Deutsche Chir., 1896, V. 47. Borggreve and Hessel: Diss. Marburg, 1856. O. Beirn: cited by Albert, Lehrbuch, V. 3, p. 227.
109. Roubaix-Karpetschenko: cited by Albert, Lehrbuch, p. 234. Hofmokl: Wiener med. Presse, 1876 and Zentralbl. f. Chir., 1876.
110. Wilms: Arch. f. Klin. Chir., V. 69. Gruber: Virchows Arch., 1869, V. 48.
111. Sultan: Zentralbl. f. Chir., 1907. Klauber: Deutsche med. Wochenscht., 1906. Neumann: Deutsche Ztschft. f. Chir., V. 91. Lorenz: Deutsche Ztschft. f. Chir., V. 102. Lauenstein: Deutsche Ztschft. f. Chir., V. 77; Zentralbl. f. Chir., 1907.
112. Wilms: Der Ileus. Deutsche Chir., 46 g. Northnagel: Handbuch d. spez. Pathol., 1895, V. 17. Propping: Mitt. a.d. Grenzgebieten, 1910, V. 21. Knapp: Inaug. Diss. Heidelberg, 1915.
113. Propping: Dieterichs cited in Chir. Kongresszentralbl., 3, p. 873.
114. Heidenhain: Arch. f. Klin. Chir., v. 55, p. 211 and Deutsche Ztschft. f. Chir., V. 43.
115. Maydl: Ueber Darmkrebs Wien., 1883. Bayer: Arch. f. Klin. Chir., 1898, V. 57, p. 233.
116. Weiss: Arch. f. Klin. Chir., 1904, V. 73, p. 839. v. Greyerz: Deutsch Ztschft. f. Chir., 1905, 77, p. 57. Kreuter: Arch. f. Klin. Chir., 1903, V. 70.
117. Anschutz: Arch. f. Klin. Chir., 1902, V. 68, p. 195.
118. Dreyer: Munch. Med. Wochenscht., 1912, No. 34.
119. cf. Rost: Munch. Med. Wochenscht., 1912, No. 38.
120. v. Greyerz and Shimodeira: Brun's Beitrage z. Chir., 1911, V. 22, p. 229.
121. Kocher-Prutz: Arch. f. klin. Chir., 1900, V. 60.
122. Qurin: Arch. fr. klin. Med., V. 71, p. 79.
123. Oppenheim: Deutsche med. Wochenscht., 1902.
124. Stadler and Hirsch: Intraabd. pressure Mitt. a.d. Grenzgebieten, 1906, 15, p. 448.
125. Albu: Ueber die Auto intoxicationen des Intestinaltraktes, Berl., 1895, Lit.
126. Sick: Deutsch Ztschft. f. Chir., V. 100.
127. Borsieky and Genersich: Bruns Beitrage z. klin. Chir., V. 36, p. 448. Nikolaysen: Studien over Aethiologie og. Pathologien of Ileus, 1895. Nesbieth: J. Exp. Med., 1899. Kukula: Arch. f. klin. Chir., V. 63, p. 773. Albeck, Ileus Arch. f. klin. Chir., V. 65, p. 569.
128. Magnus-Alsleben: Hofmeister. Betr. z. chem. Physiol., 1904, V. 6, p. 502. Falloise: Arch. intern. de Physiol., 1907, V. 5, p. 159.
129. Boruttau and Braun: Deutsche Ztschft. f. Chir., 1908, 96, p. 544.
130. Garnier: Compt. rend. d. l. soc. de Biol., 1905, V. 57, p. 388.
131. Roger: Compt. rend. d. la soc. de Biol., 1906, V. 58, p. 666, p. 675.
132. Mc Lean: Ann. of Surg., 1914, 59, p. 407.
133. Sauerbruch and Heyde: experim. Ileus. Ztschft. f. exp. Pathol. u. Therapie, 1909, V. 6.
134. Kirschstein: Deutsche Med. Wochenscht., 1889, p. 1000.
135. Wilms: Munch. med. Wochenscht., 1910, No. 5. Leuenberger: Munch. med. Wochenscht., 1910, No. 14.
136. Mauthner and Pick: Munch. Med. Wochenscht., 1915, p. 1142.
137. Crile: Revue de chir., 1914, No. 1, and J. A. M. A., 1913 and 1916.

138. Mummery: *Lancet*, 1907; *Brit. med. journ.*, 1908.
139. Mann: *Surg. Gyn. and Obst.*, V. 21, No. 4. Seelig and Lyon: *J. A. M. A.*, 1909, July. Malcolm: *Lancet*, 1907.
140. Brown: *Practitioner*, 1910.
141. Yandel Henderson: *Berlin. klin. Wochenscht.*, 1913, V. 50, p. 1938 u. 1989.
142. Ephraim and Janeway: cited in *Chir. Kongresszentralbl.*, 3, p. 2.
143. Short: *Brit. journ. of Surg.*, 1913, V. 1, p. 114 and *Lancet*, 1914, 186, p. 731.
144. Cobbet and Valte: cited by Short, *Lancet*, 1907.
145. Moty: *Revue d. chirurgie*, 1890, p. 878.
146. Morgagni: *De sedibus et causis morborum*, Lit. 51.
147. Longuet: *Bullet. d. la soc. anat. de Paris*, 1875, p. 799. Beck: *Deutsche Ztschft. f. Chir.*, 1879, V. 11, u. V. 15.
148. Sauerbruch: *Mitt. a.d. Grenzgebieten*, 1903, V. 12, p. 93.
149. Ferrier and Adam: *Franz. Chir. Congr. Lyon.*, 1894. Eichel: *Brun's Beitrage z. klin. Chirurgie*, 1898, V. 22, p. 219. Curtis: *Am. Journ. of Med. Science* 1887, V. 44. Thommen: *Arch. f. klin. Chir.*, 1902, V. 66.
150. Hertle: *Bruns Beitrage z. klin. Chir.*, 1907, V. 53, p. 257, Lit.
151. Bunge: *Brun's Beitrage z. klin. Chir.*, 1905, V. 47, p. 771.
152. Kempf: *Deutsche Ztschft f. Chir.*, 1908, V. 93, p. 524 (lit.).
153. Petry: *Brun's Beitrage z. klin. Chir.*, 1896, V. 16, p. 555.
154. Andrews: *Surg. Gyn. and Obst.*, V. 12.
155. Strohl: *Soc. de med. de Strassbourg: Gaz. med. de Strassbourg*, 1848.
156. A. Neumann: *Deutsche Ztschft. f. Chir.*, 1902, V. 64, p. 158.
157. Chaput: *Bull. et mem. de la soc. de chir. de Paris*, 1895, p. 230.
158. R. Neumann: *Brun's Beitrage*, V. 43, p. 676.
159. Prutz: *Deutsche Chir.*, 46, K.
160. Matthes: *Zeitschft. f. med. Beamte*, 1904, V. 17, p. 837. Aldrich: *Annal. of surg.*, 1902, p. 343.
161. Mc Cosh: *Med. and surg. Rep. Presbyt. Hosp.*, 1902, N. Y.
162. Zur Verth: *Munch. med. Wochenscht.*, 1910, p. 169.
163. Rech: *Ergeb. d. Chir.*, 1913, V. 7. Lit: s. bei Neutra. *Zentralbl. f. d. Grenzgeb.*, 1902, V. 5. Prutz: *Deutsche Chir.*, 1913, 46. Zesas: *Zentralbl. f. d. Grenzgeb.*, 1910, 13.
164. Litten: *Virchows Arch.*, 1875, V. 63.
165. Virchow: *Ges. Abhandlungen*, 1856, p. 420, etc. Cohnheim: *Untersuchungen ueber d. embolischen Prozesse*, Berlin, 1872.
166. v. Recklinghausen: *Deutsche Chir.*, 1883. Cohn: *Klinik der embolischen Gefasskrankheiten*, 1860, Berlin.
167. Bier: *Virchows Arch.*, V. 147 u. 153.
168. Sprengel: *Deutsch. Chirurgenkongress*, 1902 and *Arch. f. klin. Chir.*, 1902, V. 67.
169. Niederstein: *Arch. f. klin. Chir.*, 1906, V. 85, p. 410 u. 1909, V. 98, p. 188.
170. Marek: *Deutsche Ztschft. f. Chir.*, 1907, 90.
171. Mayo Robson: *Brit. med. Journ.*, 1897, 2, 77.
172. Wilms: *Munch. Med. Wochenscht.*, 1901, No. 32.
173. Rydiger: *Berlin. klin. Wochenscht.*, 1881 und *Deutsche Ztschft. f. Chir.*, V. 21, p. 546. Madelung: *Arch. f. klin. Chir.*, 1882, V. 27, p. 277.
174. Schloffer: *Mitt. a.d. Grenzgebieten*, 1900, V. 7, p. 1 and 1905, V. 14, p. 251.
175. Busse: *Arch. f. Klin. Chir.*, V. 83.
176. Payr: *Zentralbl. f. Chirurgie*, 1904 and *Deutsch. Chirurgenkongress*, 1907.
177. Schmorl: *Path. anat. Untersuch ueber Puerperaleclampsia*, Leipzig, 1893; *Gynak-Kongress*, 1901, *Arch. f. Gyn.*, V. 65.

178. Bouisson: Arch. de med. exper., Nov., 1889, p. 843.
179. Sprengel: Lit. Deutsche Chir., 1906, 46 d.
180. Wilms: Zentralbl. f. Chir., 1909, p. 1041.
181. Koerte: Freie Ver. d. Chir., Berlins, 1909.
182. Koester: Deutsche med. Wochenschrift, 1898, p. 325.
183. Mattes: Med. Klin., 1906, p. 397.
184. Trendelenburg: Deutsche med. Wochenschrift., 1899.
185. A. Hoffmann: Bruns Beitrage, 1910, V. 69, p. 701.
186. Baum: cited by Weil in Ergebn. d. Chir., V. 2.
187. Franke: Deutsche Zeitschrift. f. Chir., 1912, V. 119.
188. Lit. see Sprengel: Deutsche Chir., 1906, No. 46 d.; Koerte im Handbuch d. pract. Chir. Weil, Ueber akute frei Peritonitis, Ergebn. d. Chir., 1911, V. 2, p. 278.
189. Weil: Die akute freie Peritonitis im Ergebn. d. Chir., 1911, 2, p. 308.
190. Heyde: Med. Klin., 1908; Bruns Beitrage, 1911, 76.
191. Runeberg: Studien uber die bei perit Affekt. append. Ursprunges vorkommenden Bakterienformen, Berlin, 1908. Friedrich- Arch. f. klin. Chir., V. 68.
192. Heile: Mitt. aus d. Grenzgebieten, 1911, 22, p. 58.
193. Haim: Arch. f. Klin. Chir., 1906, 78, p. 82. Cohn: Arch. f. klin. Chir., 85.
194. Wieland: Mitt. aus d. Kliniken d. Schweiz, 1895, V. 7, 2 R.
195. Cushing and Livingood: cited by Koerte in Handbuch d. prakt. Chir., 1913, V. 3, p. 48.
196. Meisel: Bruns Beitrage, V. 40, p. 529. Danielsen: Brun's Beitrage, V. 54.
197. see Schmieden: In 'Borchard-Schmieden Lehrbuch d. Kriegs chirurgie, Leipzig, 1917.
198. Friedrich: Arch. f. Klin. Chir., V. 95.
199. Brunner: Bruns Beitrage, V. 40, p. 51.
200. Zesas, Denis: Ueber kryptogenetische Peritonitiden, v. Volkmanns Sammlung klin. Vortrage, 1912, No. 515.
201. Bonneken: Virchows Arch., V. 120. Engstrom: Ztschft. f. Geb. u. Gyn., 1897, V. 36. Rovsing: Zentralbl. f. Chir., 1892, No. 32. Schloffer: Bruns Beitrage, 1895, V. 14, p. 813. Ritter: Diss. Gottingen, 1890. Ikonnikof: Annal de 'l inst. Past. 23, p. 921. Tavel-Lanz: Mitt. aus Kliniken usw. d. Schweiz, 1893, 1, Part 1. Garre: Fortsche d. Med., 1886, p. 486. Arnd: Mitt. aus Kliniken usw. d. Schweiz, 1 Reihe, Part 4.
202. Bail: Arch. f. Hyg., 1897, V. 30, p. 348.
203. Pansini: Zieglers Beitrage, 1893, V. 12. Kocher: Arch. f. klin. Chir., 23.
204. Karlinski: Prager med. Wochenschrift., 1890.
205. Neisser: Zeitschrift. f. Hyg., 22, p. 12. Buchbinder: Deutsche Ztschft. f. Chir., V. 55, p. 458.
206. Erkes: Zentralbl. f. Chir., 1918, p. 97. Lennander: Nystrom Ztschft. f. klin. Med., V. 43. Langemaak: Brun's Beitrage z. klin. Chir., V. 37.
207. Rohr: Mitt. a.d. Grenzgeb., V. 23, p. 659.
208. Jensen: Arch. f. Klin. Chir., 1903, V. 69 and 70, p. 110, Lit.
209. Krogius: v. Volkmanns Sammlungen Klin. Vortrage, No. 467-468.
210. Burchhardt: Bruns Beitrage, 1901, V. 30, p. 731.
211. Peiser: Bruns Beitrage, 1907, V. 55, p. 484.
212. Grawitz: Charite Annalen 11, Jahrg., 1806, p. 770 and Virchows Arch., 1889, 116, p. 116.
213. Pawlowski: Virchows Arch., 1889, 117, p. 469.
214. Wallgreen: Lit. Zieglers Beitrage, 1899, 25, p. 206.

215. Reichel: Deutsche Zeitschrift. f. Chir., 1890, 30, p. 1.
216. Walthard: Arch. f. exp. Pathol., 1891.
217. Voelcker: (second infect. in infect. hernia), Bruns Beiträge, 1911, V. 72, p. 647.
218. Pfeiffer-Kolle: Ztschft. f. Hyg. u. Infect-Krankh., 1896, 21, p. 203. Isaëff: Zeitschft. f. Hyg. u. Infect. Krankh., 1894, 16, p. 287. Bordet: Annales de l' institut. Pasteur, 1897, 1, p. 177.
219. Notzel: Arch. f. klin. Chir., 1898, V. 57, u. 81.
220. Canon: Deutsche Ztschft. f. Chir., 1908, V. 95, p. 21.
221. Peiser: Brun's Beiträge, z. klin. Chir., 51, p. 681.
222. Metschnikoff: Immunität bei Infektionskrankheiten Deutsche v. J. Meyer, 1902 und die Lehre von d. Phagozyten usw. in. Kolle Wassermanns Handbuch der pathog. Microorganismen., 1913, V. 2, 2nd Edit.
223. Clairmont and Haberer: Arch. f. klin. Chir., 1905, 76, p. 41.
224. Metschnikoff: Annales de l' institut Pasteur, 1895, 369.
225. Bordet: Annales de l' institut Pasteur, 1897, 11, p. 177.
226. Haukin: Zentralbl. f. Bact., 1892, 12, p. 777 u. 809 u. 1893, V. 15, p. 852. Schattenfroh: Arch. f. Hyg., 1897, V. 31, p. 1. Buchner: Munch. med. Wochenschrift., 1894, p. 717.
227. Glimm: Deutsche Ztschft. f. Chir., V. 83.
228. Moskowitz: Arch. f. klin. Chir., 1904, V. 72, p. 773.
229. Pfeiffer and Wassermann: Ztschft. f. Hyg., 14, p. 46.
230. R. Stern: Ztschft. f. klin. Med., 1891, V. 18. Schrader: Deutsche Ztschft. f. Chir., 1903, V. 70, p. 421. R. Pfeiffer: Ztschft. f. Hyg., V. 16, 18, 20.
231. Heinecke: Arch. f. Klin. Med., 1901, V. 69, p. 429.
232. Bauer: Krankheiten d. Peritoneum in Ziemssens Handbuch, V. 8.
233. Friedlander: Arch. f. Klin. Chir., 1904, 72, p. 196.
234. Strehl: Arch. f. klin. Chir., 1905, 75, p. 711.
235. Perthes: Chirurgenkongress, 1900, p. 112 f.
236. v. Lichtenberg: Ueber die Kreislaufstörungen bei Peritonitis Wiesbaden, 1909.
237. Askanazy: Verhandt. d. Deutsch. Pathol. Gesellschaft, 3.
238. Walbaum: Wiener med. Wochenschrift, 1902, V. 37.
239. Braun und Boruttau: Deutsche Ztschft. f. Chir., 1908, V. 96, p. 544. Clairmont and Ranzi: Deutsche Ztschft. f. Chir., V. 33, p. 52.
240. Sprengel: Die Appendizitis Deutsche Chir., Lief., 1906, 46 d.
241. Henle: cited in Nothnagel's Handbuch, V. 17, p. 204.
242. Volcker: Lit. see Volcker, Bruns Beiträge, 1911, V. 72, p. 633 and Kroher: Deutsche Ztschft. f. Chir., 1915, V. 134. Chrobak: Wiener klin. Wochenschrift, 1906.
243. cf. Iselin: Zentralbl. f. Chir., 1911; Mitt. aus d. Grenzgebieten, V. 23 and Bruns Beiträge, 1916, 102.
244. Rotter: Arch. f. klin. Chir., 1910, V. 93, p. 1.
245. Wells: cited by Proot, Geschichte d. Drainage, 1884. Nussbaum: cited in Proot. Geschichte d. Drainage, 1884. Olshausen: Ztschft. f. Gyn., 1902, 48. Mikulicz: Sammlung klin. Vorträge, 1885, 262-264.
246. Propping: Arch. f. klin. Chir., 1910, V. 92. Rehn: Arch. f. klin. Chir., 1902, V. 67. Noetzel: Brun's Beiträge z. klin. Chir., 1905, V. 46 u. 47 u. Arch. f. klin. Chir., 1909, V. 90.
247. Torek: Med. Record, 1906. Buchanan: Med. Record, 1911. Scheidtman: Deutsche med. Wochenschrift., 1912. Morris: Med. Record, 1902. Clark: lit. see Kroher, Deutsche Zeitschrift. f. Chir., 1915, 134.



248. Wilms: Munch. med. Wochenscht., 1916.
249. Virchow: Virchows Arch., 1853, V. 5, p. 339.
250. Payr: Naturforscherversammlung Wien, 1913 (chir. Sect.).
251. Rost: Deutsche Zeitscht. f. Chir., V. 125 u. 127.
252. Bittorf: Grenzgebiete, 1909, V. 20, p. 150.
253. Rosenheim: Ztscht. f. klin. Med., 54 u. Deutsche med. Wochenschrift, 1909
254. Mylard: Brit. med. Journ. March, 1907, p. 484.
255. Zeidler: Mitt. a.d. Grenzgebieten, V. 5, p. 606. Riedel: Arch. f. klin. Chir., 1898, V. 47, Chirurgenkongress. Payr: Arch. f. klin. Chir., 1905, V. 77, p. 671. Terrier: Bull. et. mem. la soc. de chir. de Paris, 1902, p. 467. Lequeu: Gaz. des hopitaux, 1895, p. 1328. Quenu-Walter-Routier: Bull. et. mem. de la soc. de chir. de Paris, 1902, p. 712. Poirier: Bull. et mem. de la soc. de chir. de Paris, 1902, p. 472 (discussion). Brunn: Deutsche Ztscht. f. Chir., 1905, V. 76. v. Bergmann: Arch. f. Klin. Chir., V. 61, p. 921. Berard and Patel: Revue de chir., 1903, p. 590.
256. Collective References: Isler Zentralbl. f.d. Grenzgebiete, V. 12, 18-19; Pick, Ztscht. f. klin. Med., 1896, V. 29; Esau, Deutsche Ztscht. f. Chir., V. 125.
257. Rehn: Handbuch f. prakt. Chir., 1913, V. 2, p. 932.
258. Corner: Annals of surg., 1910.
259. Corner: Brit. med. Journ., 1913, p. 325.
260. Funke: cited by Sprengel, Appendicitis, Deutsche Chir., 46 d. p. 49.
261. Robinson: Compt. rend. hebdom. des seances de l'acad. des sciences, 1913, V. 107, p. 790. Heile: Brun's Beitrage, V. 93. Chirurgenkongress, 1914, p. 247.
262. Appendicitis: Lit. Lanz: Brun's Beitrage, 1903. Klein: ibid., 1904, Adriaux, Grenzgebiete, 1902, V. 7; v. Hartsemann, ibid., 1903, Sommenburg, Pathologie u. Chir. d. Perityphlitis, Leipzig, 1905; F. C. W. Vogel; Sprengel: Deutsche Chir., V. 46. Aschoff: Die Wurmfortsatzentzündung. Jena, 1908, u. Ergebn. d. inneren. Med., 1912, V. 9. Meisel: Bruns Beitrage, 1903, V. 40. Schrumpf, Grenzgebiete, 1907. Blinddarmhanges, Jena, 1910. V. Brunn, Ergebn. d. Chir., 17. Kretz ibid.; Noll, ibid. Winkler, Die Erkrankungen d. u. Orthop, 1911, V. 2.
263. Tavel-Lanz: Rev. de chir., 1904. Heile: Chirurgenkongress, 1909.
264. Kretz: Wiener klin. Wochenscht. 1900; Verh. d. Deutsch. pathol. Ges. 1906, Mitt. a.d. Grenzgebieten, 1907 and 20, 17; 1909; Ztscht. f. Heilkunde, 1908, V. 28.
265. Muhsam: Deutsche Ztscht. f. Chir., 1900, 55. Winkler: Erkr. d. Proc. vermiciformis. Jena, Fischer, 1910. Stoeber and Dahl: Mitt. a.d. Grenzgebieten, 24. Ribbert: Deutsche Med. Wochenscht., 1885. Roux-Roger-Losne: Rev. de med., 1896, V. 16. Charrin: Compt. rend. Soc. de Biol., 1897. Anghel: These de Paris, 1897. Beausse: Bull. de la soc. anat. de Paris, 1897. Paine: Lancet., 1911, Brit. med. Journ., 1911. Adrian: Mitt. aus d. Grenzgebieten, 1901, V. 7, 9.
266. Ten Horn: Arch. f. Klin. Chir., 109, Part 2.
267. Dieulafoy: Acad. de med., 1896.
268. Klecki: Annales de l'inst. Pasteur, 1895 u. 1899, 9 u. 11.
269. Meisel: 33 Deutsches Chirurgenkongress, 1904.
270. Klauber: Munchener med. Wochenscht., 1909, p. 451.
271. Brunn: Mitt. a.d. Grenzgebieten, 1909, V. 21.
272. McLean: Mitt. aus d. Grenzgebieten, 1909, V. 21.
273. Hoenck: Ueber die Rolle d. Lymphaticus bei Erkrankung d. Wurmfortsatzes Jena. Fischers Verlag, 1907.

274. Sonnenburg: Perityphlitis 1913, p. 108, 7 edit., F. C. W. Vogel.
275. Kafemann: Deutsche med. Wochenschrift, 1911.
276. v. Redwitz: Brun's Beitrage, 1913, V. 87.
277. Rippert: Virchows Arch., 1893, V. 132 and Deutsche med. Wochenschrift., 1903, inflammation is accepted. Zuckerkindl: Anat. Hefte, 1894. Schmorl: Münchener med. Wochenschrift., 1910, V. 17, p. 936. Oberdorfer: Grenzgebiete, 1906, V. 15.
278. Miloslavich and Namba: Grenzgebiete, 1912, V. 24.
279. Aschoff: in Deutsche med. Wochenschrift., 1906, p. 985.
280. Riedel: Arch. f. klin. Chir., 1902, 66.
281. Payr: Arch. f. klin. Chir., 1907, V. 84.
282. Moynihan: Brit. med. Journ., 1910, p. 241.
283. Paterson: Lancet., 1910, p. 708.
284. Silhol: 24th French surgical congress, 1911. Ewald: 28 Deutscher Chirurgenkongress, 1899, p. 685.
285. Sick: Zeitschrift. f. Chir., V. 70. Jordan: Arch. f. klin. Chir., V. 69. Fischl: Prager med. Wochenschrift, 1904.
286. Ghedini: La Clin. chir., 1905. von Brenner: Wiener klin. Wochenschrift., 1907. Extensive Resect. of ileum collected by Kukula: Arch. f. Klin. Chir., 1900, V. 60, p. 912. Nigrisoli: Nuovo Raggogl. med., 1902. Pauchet: Gaz. med. de Picardie, 1905. Axhausen: Mitt. aus d. Grenzgebieten, 1910, V. 21.
287. Denk: Mitt. aus d. Grenzgebieten, 1911, V. 22.
288. Trzebicki: Arch. f. klin. Chir., V. 48, p. 54. Monari: Brun's Beitrage z. Klin. Chir., 1896, V. 16.
289. Blayney: Brit. med. Journ., 1901. Soyesima: Deutsche Ztschft. f. Chir., 1911, V. 112. Diliberti Herbin: Gaz. med. ital., 1903. Albu: Mitth. a. d. Grenzgebieten, 1909, V. 19 and Berlin. klin. Wochenschrift., 1901.
290. Lieblein: Mitt. aus d. Grenzgebieten, V. 23, part 1.
291. London: Zeitschft. f. physiol. Chemie, V. 49.
292. Stasoff: Bruns Beitrage z. klin. Chir., 1914, V. 89.
293. Ziesch: Deutsche med. Wochenschrift., 1909, p. 739. Riva-Rocci: Gaz. med. di Torino, 1896. Nagano: Bruns Beitrage, z. Klin. Chir., V. 38. Erlanger und Hewlett: Am. J. of Physiol., 1901, V. 6. Albu-Lexer: Berliner. klin. Wochenschrift., 1901, p. 1248.
294. Brugsch: Ztschft. f. klin. Med., 58, p. 518.
295. Flint: Bull. of John Hopkins Hosp., 1912.
296. Evans and Brenizer: Bull. of John Hopkins Hosp., 1907, p. 477.
297. Barker: The Lancet., 1905.
298. Bauer: Ergebn. d. chir., 1912, V. 4, p. 573.
299. Rost: Münch. med. Wochenschrift., 1918, No. 5.
300. Ludloff: rectal prolapse, Arch. f. klin. Chir., 1899-1900, V. 59 u. 60.
301. Beresnegowsky: Arch. f. klin. Chir., 1910, V. 91, p. 627.
302. Bell and Hirschberg: Berlin. klin. Wochenschrift., 1894, No. 14.
303. Waldeyer: Lehrb. d. topogr. chir. Anat., 1899.
304. Esmarch: Deutsche Chir., V. 48.
305. Ziegenspeck: Arch. f. Gynakol., 31. Trager: Arch. f. Anat. (u. Physiol.), 1897. Wenzel: Deutsche Ztschft. f. Chir., 1905, V. 76, 19. Waldeyer, Zuckerhandl: Deutsche Ztschft. f. Chir., 1891, V. 31, p. 590.
306. Mummery: Brit. med. Journ., 1907, p. 2439.
307. Jeannel: Legons. de clinique chir. faites a l'Hotel-Dieu de Toulouse, 1897.
308. Lenormant: Le prolapsus de Rectum These de Paris, 1903.

## CHAPTER VIII

### KIDNEYS, BLADDER, MALE GENITALIA, HYPOPHYSIS

In unilateral renal disease, it is always very important to make sure that the other supposedly healthy kidney is really functionally efficient. To determine this, methods are frequently used which depend on the appearance of foreign substances in the urine after they have been administered through various routes to the patient (1). These methods presuppose that endogenous and foreign substances are eliminated by the same anatomical part of the kidneys, and also that the different chemical substances all pass through the same place in the renal system. Since this supposition is incorrect, all the kidney functional tests which depend on the elimination of foreign substances, colors, salts, etc., have only comparative values although this does not condemn their practical usefulness.

But what do we actually know of the "*microscopic*" function of the kidneys, *i.e.*, of the locality and the manner in which the elements of the blood are excreted? The theory of Ludwig and that of Heidenhain still hold the center of interest. Ludwig claimed that renal function is a pure filtration process consisting of the formation of urine from the blood by filtration through the glomeruli. Heidenhain believed that urine is a product of secretion of the renal epithelium, especially of the convoluted tubules. The numerous investigations of the last decades (2), have shown that neither of these theories can claim absolute correctness; the formation of urine is an exceptionally complex process, and the excretion of the different substances which constitute it probably occurs in different parts of this glandular organ. Perhaps even part of the water excreted is again reabsorbed in the uriniferous tubules, but all these factors are not as yet clear (3).

[In passing, it may be useful to consider the so-called "modern theory" of renal secretion. The details may be found in the monograph by Cushny. The substances of the blood are divided into two classes in reference to their excretion by the kidney, the threshold and the no-threshold bodies. That is, there are substances which are excreted as long as any are left in the blood, in other words, in proportion to their absolute amount in the plasma. Others, the threshold bodies, are excreted when their amount in the blood exceeds a certain threshold value. An example of a no-threshold body is urea, but while it cannot be proved directly

for this substance, because it is continuously replaced in the blood, it nevertheless resembles in its excretion, other substances which can be demonstrated to be no-threshold bodies. Dextrose, chloride and sodium are at the other extremity, and when their amount in the plasma falls below a certain threshold, they cease to be excreted.

The recent advances in physical chemistry have shown that Ludwig's theory cannot account for kidney function, mainly because the known physical force, *i.e.*, the blood pressure, is not adequate to filter off a urine of greater osmotic pressure from the blood plasma. The blood pressure can, however, filter off the constituents of the plasma with the exception of the proteins to which the capsular membrane is impermeable, and therefore, what amounts to a deproteinized plasma can pass through. This is very different from the final urine, for the proportions of the solids have changed. This is accounted for by assuming that in its passage through the tubules, water and certain other of its constituents are absorbed by the living epithelium. To put it briefly: The threshold bodies are taken up by the vital activity of the epithelium and returned to the blood in the proportion determined by their normal values in the plasma, while the no-threshold bodies are allowed to proceed further and be excreted.

The known physical forces are therefore supplemented by the necessary addition of this unknown force which discriminates and returns to the blood, substances which ensure its normal composition.

It might be mentioned that the evidence for reabsorption has been entirely indirect until the recent work of Wearn has given direct data. He has succeeded in introducing a very fine capillary pipette into the capsular space of a frog's kidney under indirect illumination and direct vision. Glucose was found in seven instances in glomerular urine and not in bladder urine. The same was true of chlorides in four frogs. The results are offered as proof of reabsorption in the tubules and as strong evidence of glomerular filtration (4)].

It would be of the highest practical importance if the salts, colors and other substances, including water, used for *functional tests*, could be grouped according to the part of the kidney from which they are excreted, for by investigating the elimination of a member of each group, it would be possible to obtain a true picture of the functional ability of a kidney. Attempts have frequently been made to classify renal diseases in this way, hoping primarily, to define clearly the different forms of Bright's disease. The excretion of these various substances was measured *in vivo*, and later controlled by autopsy to discover which part of the kidney was especially affected. It was supposed that by reasoning backward, the particular part of the tubular system in which these different substances were excreted could



be found. This idea seems reasonable, but nevertheless, it has not helped to mold a uniform opinion. Quite to the contrary, while Koranyi and his pupils think that the excretion of water and sodium chloride takes place in the glomeruli, while nitrogen excretion is assigned to the convoluted tubules, Fr. Muller, and Monakow (5), believe the reverse. Schlayer (6) attempted to solve this question by systematic experiments. He produced nephritis in animals by various poisons and believed that two forms occur. The first, "vascular nephritis," primarily affected the vessels, and led to a complete suspension of the secretion of water, for instance, after arsenic and cantharidin. The second, a "tubular" form, first injured the epithelium, and soon showed diminution of sodium chloride and potassium iodide elimination, but the excretion of water was not diminished; on the contrary, polyuria was present. The excretion of milk sugar was not impaired, and he believed, therefore, that a delay in milk sugar excretion would suggest vascular injury. Many objections which cannot be detailed here were raised to these experiments (see Gross (3)), particularly to their application to human pathology. Volhard ((2) p. 1182) concluded that glomeruli and tubules excrete the same substances, although in different concentrations, and that the specific action of the glomeruli consists in dilution, while the specific action of the tubules consists in concentration.

Topical function tests of the kidneys seem almost hopeless, and practical surgery has been content to use methods which give an idea of the total excretory ability of a kidney, without considering a possible affection of separate parts. The usefulness of most of these functional tests is, as already stated, based merely on the "sum total" of practical experience. Those methods are useful which consider the specific activity of the glomeruli and the tubules, testing, therefore, whether the renal concentrating power is sufficient, and whether the kidney is able to eliminate water quickly when given in excess (Gottstein (1)).

The drink test first advised by Albarran (7) is now little used in surgical renal diseases. The reasoning is this: with a dry diet, the specific gravity of urine quickly increases; and it is a sign of renal insufficiency if the kidneys cannot eliminate concentrated urine. But in addition to changes in concentration, we often consider polyuria itself a sign of renal insufficiency; and as an example, the polyuria in patients with prostatic hypertrophy need only be mentioned.

Other methods attempt to determine the functional ability of each separate kidney in an even more general manner. It has been proposed to examine the secretion of the separate kidneys to discover if equal quantities of urea or chlorides are excreted under the same experimental conditions. The functional ability of a single kidney may also be tested

by determining whether colors, which are usually administered to the patient intramuscularly, reappear in the urine in a certain time and in a certain quantity. Phloridzin injections have been used, after which a healthy individual excretes sugar, as is well known, and this constitutes a true renal glycosuria. The diseased kidney excretes less sugar or its excretion is delayed. Finally, in unilateral renal diseases, it may be necessary to determine only whether the total ability of both kidneys is sufficient. For this purpose, the molecular concentration of the blood is determined by the lowering of the freezing point or by other physico-chemical methods. This is exceptionally constant under normal conditions and rises only if the excretion of certain urinous substances becomes impaired.

The activity of the kidneys, like that of other glandular organs, can be much influenced by their *nerve supply*; and they, like other glands, possess a double innervation: the major and minor splanchnic nerves and the vagus (8). (In regard to the ramification of the renal nerves see Disse, Smirnow, Renner (9)). There are also sympathetic ganglion cells in the kidney itself, which explains why urine is secreted, and why the kidney shows a certain adaptability to every possible functional stimulus even after all afferent nerves are severed, as shown for example, by Lobenhöfer (10) who succeeded in suturing the vessels of one kidney to the splenic vessels. But the afferent nerves are not altogether without influence. Although cutting and stimulation of the vagus have not given constant results, Meyer, Jungmann and Eckhard (11) found that section of the splanchnic nerve caused polyuria; while irritation was followed by alterations in urine secretion (12); a statement verified by other workers. These sympathetic branches pass to the celiac ganglion, and this is probably the first station, where reflex stimuli can be transferred from one side to the other. Another station can be demonstrated in the spinal cord, but the further course of these tracts toward the cerebrum is not known in detail. Gaetani's (13) statements that unilateral renal extirpation in the rabbit leads to demonstrable changes in both anterior columns of the spinal cord as far as the cerebral base require further investigation.

Eckhard showed that polyuria can be induced by puncturing the medulla, somewhat lateral to the area used for the Claude Bernard sugar puncture, and Jungmann and Erich Meyer have found in addition that a tremendous increase of sodium chloride elimination results from this medullary lesion. For this reason they speak of a "salt-puncture." But it is not quite clear at present whether these phenomena are caused by some form of direct nerve stimulus (Jungmann, Meyer), or indirectly, by activation through some hormone, *i.e.*, adrenalin or hypophysin, which in its turn stimulates the kidneys through the blood (see Volhard (2)).

The question whether the nerves described should be accepted as *secretory nerves*, or whether they influence urinary secretion indirectly by *vasomotor activity* is decided by microscopical anatomical investigations showing that the kidney is probably supplied by *secretory nerve fibres*, in addition to its abundant *vasomotor nerves* (9). The kidney capsule, the pelvis and also the renal connective tissue, contain sensory nerve filaments according to Meyer and Jungmann, while the musculature of the pelvis contains motor fibres. The kidney becomes painless after cutting the spinal cord at the eighth to ninth dorsal level, while cutting the splanchnic nerve has no influence on its sensitivity (14).

It is not certain that the *attacks of pain* in different renal affections are due only to pulling of surrounding tissue as stated by Wilms (15). Even if the patient does not feel the introduction of the ureteral catheter, he usually feels a stabbing pain when the wall of the pelvis is touched (see also (16)), and this pain can become very severe if, for instance, the pelvis is filled for pyelography. For this reason it must be assumed that these sensory nerves transmit pain sensations. The stimuli are frequently transferred to spinal nerves which explains the "radiation" of the pain in renal colic.

This nerve supply is of particular interest because it forms the foundation for studying *reflex anuria*, which occurs not rarely in surgical renal and ureteral diseases. Such reflex anuria is observed chiefly when a calculus obstructs an ureter; and according to Goetzl and Israel (17) it is caused by an increase of intrarenal pressure. In the animal experiments of Goetzl, anuria was rare; and this has been confirmed by other workers (18). But Cohnheim and Roy (19), by irritation of the sciatic nerve, and Masius (19) by vagus irritation, obtained anuria. In both cases, according to general opinion, this is due to a reflex vessel spasm. But nothing certain is known in the matter; and a spasm would hardly explain an anuria of some duration; Ghiron (20) also, who observed the living organ under a light cone, could not demonstrate vessel spasm, but he found a delayed coloring of the striated border after injection of aniline blue. Meyer and Jungmann (21) produced reflex anuria fairly regularly by irritating the bladder and ureter, after previously cutting the splanchnic nerve. Jenckel (22) reports a very interesting case, appropriate in this connection, in which after unilateral nephrectomy a complete anuria developed which could not be explained at autopsy even microscopically.

In interpreting all these so-called reflex disturbances of renal function, it is important to know the quantity, quality and time of *normal secretion*. Cystoscopic data is always somewhat uncertain because the instrument acts as a renal irritant, and because ureteral catheters never fit closely enough to prevent the escape of urine around them. Animal experiments



relating to this question have been made by Kapsammer (23), Pflaumer (8) a.o. They hardly give an accurate picture of the normal conditions, however, since in all these experiments considerable manipulation is unavoidable. The observations made in cases of exstrophy of the bladder, reported by Luter, and Meyer, also Allard (24) are more useful. Accordingly, the urine usually escapes alternately from the two ureteral orifices; it is only during more marked diuresis that the flow proceeds irregularly. The quantity poured out by each ureter is not the same during short periods of observation; during longer periods, the differences diminish. The same is true of the composition of both urines. But if the kidneys are functionally severely taxed, *i.e.*, by copious water drinking, the differences in the quantity and composition of the urines become greater.

Changes in posture influence renal activity (25) (8). During an upright position the kidneys secrete less than when prone, and lying on the side also seems to have its influence. It has not been determined how much of these postural variations are due to reflex influences. In addition, the ureteral movements may be influenced reflexly. In Allard's patients, a mere touch of the ureteral opening, was sufficient to interrupt their rhythmic action for minutes. The urine in the mean time collected in the pelvis, and after this pause, was discharged all the more quickly.

Pflaumer, in his experiments on animals, obtained somewhat different results. There was an increase in ureteral activity and in water secretion after touching the ureter with alcohol.

The more the bladder fills, the more the ureters contract; but water secretion diminishes and this decrease of urine formation does not depend on stasis in the ureter, but must be considered as a vesico-renal reflex (8).

Increase in water excretion (*polyuria*) which occurs normally after an abundant intake of fluids, and also after a diet especially rich in nitrogen, is observed in the most varied conditions. It is usually divided into an indirect, neurogenous, or reflex form, and into a hematogenous or nephrogenous form. Polyuria from a contracted kidney, in which of course the greater number of the glomeruli is destroyed, is a nephrogenous polyuria, and is a symptom of a certain type of renal insufficiency. From this, Fr. Muller (5) concluded that the secretion of water in the kidney must occur not only in the glomeruli, but also in the convoluted tubules.

In surgical kidney disease, it is often very difficult to distinguish these two groups and, *e.g.*, the polyuria in tuberculous nephritis (26), the so-called "clear" polyuria, is considered by some as evidence of renal insufficiency, and by others as pollacissuria, and, therefore, a purely reflex process. According to Guyon, a voluntary increase in the quantity of urine can be produced by frequent urination. Conversely "if convivial drinkers at long sessions abstain from the first voiding, they are able to retain the urine



without pain for considerable time," but after the first voiding, a flow of urine takes place which necessitates repeated urination (27). It has already been stated that a "sugar- or salt-puncture," *i.e.*, injury of the central nervous system produces polyuria, a fact which forms the experimental basis of our knowledge of the diabetes insipidus occasionally seen following head injuries.

The influence of peripheral innervation on the quantity of urine has been shown in the experiments of Rohde and Ellinger (12) in which polyuria occurred after tearing the renal nerve supply apart. The older experiments of Eckhard (11) and Knoll (11) also produced polyuria in the dog, by sectioning the splanchnic nerve. Purely reflex polyuria is occasionally caused by ureteral catheterization (11), (23). By this method of investigation, however, it is necessary to be cautious in drawing far-reaching conclusions from the quantity of urine excreted.

The production of urine during retention is always of special interest, not only for purely experimental reasons, but also because the polyuria in prostatic hypertrophy belongs to this group. Related experiments were made by Cohnheim, Albarran, Ponfick, Steyrer, Filhene and Ruschhaupt, Allard, Schwarz, Pfaundler *a.o.* (for further lit. see under "Hydronephrosis" (27)). They served in part to study the changes occurring in hydronephrosis, and in part to discover whether a reabsorption of urine actually took place in the uriniferous tubules; finally, this method of approach seemed the least disturbing in attempting to produce a graduated renal lesion. This latter viewpoint also interests the surgeon, *i.e.*, the question of the effect on function of a slight but chronic retention of urine. Unfortunately the writers have not obtained similar results. Some observed polyuria with urine of low specific gravity, others, a decrease of quantity and diminished nitrogen and sodium chloride excretion. A number of these records relate to investigations on man, but here also there is no uniformity in the findings. According to the very careful observations of Allard on a patient with exstrophy of the bladder, it seems that in unilateral obstruction, the other kidney can compensate and secrete a much larger quantity, while the test kidney produces less urine than normal. Styrrer *a.o.*, obtained similar results. But undoubtedly in most cases of hypertrophy of the prostate, the quantity of urine is greatly increased, even at a time when there is only a slight dilatation of the renal pelvis (28). Whether the frequency from vesical irritation which is usually present in the early stages of this condition, has led to marked polyuria, is not certain, but possible. As a whole, these contradictory findings have not been cleared up, but the impression is gained that the kidney responds with extraordinary sensitivity to any stimulus, and changes the quantity and composition of urine. Therefore, the end

results of our more or less clumsy experimental and operative interferences are not always uniform. The duration of the observations must also be considered.

If this *chronic retention* has gradually distended the pelvis, and thus diminished the amount of kidney tissue which is functioning, a condition arises somewhat analogous to the experimental renal atrophy, studied by many workers (29). As a rule polyuria was found, but we can only note the fact, the reasons for polyuria of whatever type, are completely unknown. The supposition of Schlayer from findings in his animal experiments, that it is due to a hyperirritability of the vessels, can not, according to Volhard, be accepted as a generalization.

Furthermore, in chronic retention, the concentrating ability of the kidneys is much disturbed (30); considerable storage of residual nitrogen is avoided by the abundant flow, but mineral constituents accumulate in the blood and lead to a lowering of the freezing point. Veil has shown that even in normal individuals the molecular concentration of the blood is increased after copious drinking, perhaps because the tissues are rinsed out more thoroughly. The blood concentration must increase all the more if the kidneys on account of chronic retention have lost the power to excrete concentrated urine. The net result of such a washing out is that the patients feel more thirsty and drink still more, thus forming a vicious circle, which finally leads to a marked desiccation quite characteristic of patients with hypertrophy of the prostate, or chronic retention from any other cause.

The question now arises, how is this disease complex related to *uremia*? Uremia means an accumulation of substances in the blood, which are normally excreted in the urine. The purest form should then be caused either by extirpation of both kidneys, or by mechanical prevention of the outflow of urine. The clinical picture is usually described as though it were a suddenly appearing condition of coma and epileptiform convulsions. But if we observe a patient with functional insufficiency, or one in whom nephrectomy has been done when the other kidney was absent, we see quite a different picture. It corresponds perfectly to what was formerly called "chronic uremia:" "The patients complain of dull headache, or a confused feeling in the head, the eyes become dim and expressionless, the lines of the face sag; they are indifferent, forgetful and fatigued. Then deep lethargy follows, and finally a few terminal convulsions"(31). The epileptiform or eclamptic convulsions generally considered as characteristic of uremia are usually absent. Is this merely due to degrees or time differences in the course of the disease? Most decidedly not; because it cannot be conceived how a more complete and quicker accumulation of urinous substances can take place in the blood than in bilateral neph-

rectomy. It follows, as was first pointed out by Ascoli (32), that every acute disease accompanied by epileptiform convulsions cannot be a result of the accumulation of urinous substances in the blood, but that these convulsions are due to some other toxins. Ascoli, who thinks of decomposition products derived from the diseased kidney itself (nephrolysins), calls this symptom complex "kidney wasting." We shall presently return to these questions.

At any rate, we must distinguish in these pathological conditions, those which are actually due to accumulation of urinous substances in the blood ("urinary toxemia" according to Ascoli), and those described above in the words of Frerich. Most surgical kidney cases die of the former of these disease complexes, *i.e.*, hydronephroses, pyonephroses, cystic kidneys, nephrectomies, etc. Although very many investigations and experiments have been conducted by numerous authors, no definite one of the urinous substances can be said to cause the symptom complex (33). Of practical importance is the fact that there is an increase of residual nitrogen in the blood in all these forms of true uremia, *i.e.*, to repeat it again, a uremia due to poisoning by urinous substances. It is not certain that this residual nitrogen contains the "toxic" substance, but it is not improbable; and this leaves the question open, of whether it is the urea or some other organic body which produces the toxic action. From the surgical viewpoint (34) it has been stated on the basis of suitable experiments, that there is a certain similarity between uremia and the toxemias produced by introducing burned tissue subcutaneously into animals. But at present, it is entirely unknown how the toxemia resulting from such protein decomposition products has anything in common with uremia, directly or indirectly.

It has also been thought that uremia could be produced indirectly only through the liver (35).

Whether there are still other factors, alone, or in combination, is entirely unknown at present, although Sauerbruch and Heyde (36) conclude from their para-biosis research, that retention of urinous substances alone cannot be responsible for the death of the animals, for they found that the removal of both kidneys of one animal, linked para-biotically to the other, caused the death of both. Consequently the animal with kidneys did not excrete sufficient toxins.

Jehn, Birkenbach, and Morpurgo (37) arrived at identical results with similar methods. But for the present, too far reaching deductions should not be made from these experiments, since we do not know from residual nitrogen determinations, how much of these urinous substances was carried through to the unoperated animal.

Opposed to this chemical conception of the toxic action of urinous sub-

stances is the physical theory of Koranyi and Lindemann (38), according to which the increased osmotic pressure of the blood serum is responsible for the clinical disturbances described.

The symptoms thought by Ascoli to be the result of "*kidney wasting*," must be sharply differentiated from this true uremia. The term is not a happy selection. It is intended to describe conditions, which, as Volhard expresses it, may occur without renal insufficiency, and which are, therefore, not directly dependent on an accumulation of urinous substances in the blood. The uremia of acute nephritis is of this type. Without doubt, the retention of urinous substances is a factor in this disease, but the characteristic attack with coma and convulsions, vomiting and headache, is not a result, since it does not occur with nephrectomy or ureteral ligation. Volhard (33) in particular points out that this triad, headache, vomiting, and slowing of the pulse, to which may be added convulsions, reminds us more of a space reducing process within the skull, and the high pressure found at lumbar puncture bears out this idea. Traube (39), years ago, thought of edema of the brain as a cause of uremic seizure, and if this belief was ignored for decades, it was only because no difference was recognized at that time between the different symptom complexes of "uremia." Traube for this reason considered all forms of uremia including that following kidney extirpation, due to edema of the brain, which was incorrect. But that it is actually present in the uremia accompanied by convulsions is shown by the pictures of Volhard. Zangemeister, by trephining (33), has actually been able to show the edema of the brain in vivo in a case of eclampsia. The same condition has been demonstrated repeatedly at operation during the convulsive attacks of epilepsy which show similarity to those of uremia.

It is naturally very difficult to say which is cause and which is effect. Volhard believes the edema of the brain in uremia is from congestion, assuming an ischæmic contraction of the cerebral arteries, with wide open veins. He supports this idea by the eye-ground findings in acute nephritis, in which there are tightly contracted arteries with dilated veins. The permeability of the vessels is also supposedly abnormal.

These vascular changes, especially the increased vasomotor irritability, always play a considerable role in the symptom complex (see "*Hypertension Theory in Eclampsia*"—Osthoﬀ, 1886), and explain the enormous increase in blood pressure and hypertrophy of the heart found in such patients. The theory of Cohnheim-Traube that the blood pressure increase is a result of increased resistance in the kidney, has been generally abandoned. But it must again be emphasized that these vasomotor disturbances are not usually encountered in surgical uremia (nephrectomy, ureteral ligation, etc.), although it is possible that the picture may be



complicated; especially in chronic cases (hypertrophy of the prostate) and naturally also in the presence of arteriosclerosis.

No positive explanation of the etiology of this "tendency to edema" and the vasomotor disturbances is, as yet, possible. Since the clinical picture gives the impression of an acute poisoning, it is natural to look for some toxic substance, and in drawing analogies, the acute uremic attack resembles most markedly the picture of anaphylaxis. For this reason the idea of a protein toxemia was frequently expressed, but the theories concerning the mechanism are most varied (40). Brown-Sequard and his pupils thought of the disappearance of an internal secretion of the kidneys. H. Pfeiffer draws analogies between uremia and anaphylactic shock, and believes he demonstrated an anaphylatoxin in the urine (33). Other writers, such as Biedl, content themselves with proving that renal extracts, especially from those organs showing nephritic changes, possess peculiar properties, *i.e.*, marked lymphagogue action, and the ability to increase the permeability of the vessels, phenomena which are also observed in uremia. When theories are carried too far, they are only misleading. It is indeed conceivable in uremic attacks, that certain decomposition products of renal origin enter the circulation and incite the attack, but this has not been proved. In fact, the process may be quite different, and far more complex than is imagined. It seems necessary to make extensive investigations of the blood of patients during uremic attacks, because it is in this fluid that we must search for the toxins. Schlayer (41) and Straub (41) did determine the acidity of uremic blood and believe it is increased, a statement disputed by some, and confirmed by others (41).

[In regard to the term "anaphylaxis," it should be remembered that many conditions are grouped under this heading in the literature and that great confusion has resulted. Wells (*Physiol. Reviews*, 1, p. 44, 1921) has clearly given the criteria in which the term should be used and suggested that "anaphylactoid" should be the name for conditions simulating true anaphylaxis. The criteria are:

1. The toxicity must depend on sensitization, *i.e.*, must not produce similar symptoms in non-sensitized animals.
2. They must be characteristic of anaphylaxis.
3. Passive sensitization with the serum of a sensitized animal must be demonstrable.
4. The bronchial spasm in guinea pigs must be relieved or prevented by atropin or adrenalin.
5. Capillary thrombosis or embolism must be excluded.
6. After recovery from anaphylactic shock, desensitization should be exhibited.

The *acid-base equilibrium*, according to present ideas, may be summed up as follows: the reaction of the blood and of the tissues as a whole remains remarkably constant. The factors determining it are, of course, the relative amounts of acids and bases present. Since direct measurements determine the hydrogen ion, *i.e.*, the acid radicle, the results of determinations are expressed in terms of the concentration of these ions, and in order to simplify the expression, the symbol Ph, or Ch, with a minus logarithm as exponent is used.

The "total" acid may be said to be composed of two varieties, the volatile, namely carbon dioxide, excreted by the lungs; and the fixed, such as are bound with phosphates, chlorides, proteins, etc., excreted mostly by the kidneys. During life there is constant production of acid, and a constant oscillation between acid and alkali, but so delicately balanced that the "total" amount of acid, *i.e.*, the H ion concentration, is kept within very narrow limits. For example, the fixed acids may be increased because of either overproduction as in diabetes, or failure of excretion as in nephritis. To keep the "total" amount of acid constant, it is necessary that the carbon dioxide be reduced in amount per cubic centimeter of blood. An estimation of its quantity will therefore discover a smaller amount. This has been termed "compensated acidosis." "Uncompensated acidosis" results when the increase of fixed acids is so great that the carbon dioxide cannot be sufficiently reduced per cubic centimeter of blood to maintain life. In other words, the "total" H ions are increased. In either of the two cases, since each unit of blood carries less carbon dioxide, it follows that to rid the body of this substance, if its production is not diminished, the individual must breathe more rapidly, or the circulation rate must be increased, or both. Hence, we have dyspnea without cyanosis.

But if by overventilation, an excessive amount of carbon dioxide is breathed off, it leaves the blood more alkaline, and it is thought that alkali is transferred from the blood to the cells and that other shifts in acid and basic salts take place. At any rate, it is clear that there are nine possibilities, the carbon dioxide of the blood may be high, low or normal, and the H ion concentration may be high, low or normal. The only condition which is normal, is where both carbon dioxide, and H ion concentration are within normal limits (see VAN SLYKE, D. D., *J. Biol. Chem.* 48, 153, 1921). It follows that accurate information of the condition of a patient at any given time must involve the determination of both the carbon dioxide and the H ion concentration of the blood.

But it must be emphasized that "acidosis," a name used very loosely, is but a symptom of an underlying cause which can oftentimes be recognized. If it is desired to treat an uncompensated acidosis, *per se*, the use of an

alkali is indicated, but an overdose is to be avoided. Alkalosis has not received as careful study as the opposite condition, but there are indications that it is also harmful. The proper dose of sodium bicarbonate may be calculated to within sufficiently narrow limits by the use of the formula devised by Palmer and Van Slyke. Assuming that sodium bicarbonate is absorbed from the gastro-intestinal tract and is distributed equally throughout the body fluids, the amount of carbon dioxide yielded from one gram of sodium bicarbonate, namely, 267 c.c., will be distributed among the fluids of the body (about 700 c.c. per kilogram of body weight) in volumes per cent., according to the formula  $\frac{267}{7W} = \frac{38}{W}$  where  $W$  = the weight in kilograms. If  $g$  grams of the alkali are given the rise in volumes per cent. =  $\frac{38g}{W}$ . Whence  $g$ , or the amount necessary to raise the carbon dioxide by  $C$  volumes per cent. =  $G = \frac{CW}{38}$  (see also *J. Biol. Chem.*, 46, p. 493, 1921).

Finally, it might be remarked that this acid-base equilibrium is so intimately dependent on other factors that L. J. Henderson has been enabled to construct a diagram on which he plots the values of the free and combined oxygen, the free and combined carbon dioxide, or carbonic acid, the serum chlorides and the hydrogen ions of the blood. If the value of any two are properly determined in a given sample of blood, the values of the others can be unequivocally placed, a fact from which the conclusion that all these six variables are involved in a single physiochemical equilibrium, can be deduced. In other words, the manner in which acids and bases are shifted, oxygen is combined or dissociated, carbon dioxide is combined or dissociated, chlorides are distributed between cells and fluid, and oxygen influences hemoglobin to be either a weak acid or a weak base, all depend one upon the other (see HENDERSON, L. J., *Blood as a physicochemical system: J. Biol. Chem.*, 46, p. 411, 1921).

The work, especially of L. J. Henderson, Van Slyke, and Y. Henderson can be consulted for details (42).]

Now *decapsulation of the kidney* has been suggested as a surgical treatment for uremia and it would perhaps be interesting to discuss the effects of this procedure (43). In that form of uremia which represents the final stage of renal insufficiency, *i.e.*, hydronephrosis, cystic kidney, etc., it is self evident that no result can be expected from this operation. Unger (44) implanted the kidney of a monkey in a case of this kind, but could not prevent death. According to the reports of some writers, renal decapsulation seems to have yielded good results in a few cases of anuria (45). On the other hand it is not astonishing that many operators report bad results. Naturally an old contracted kidney cannot be saved by decapsulation and

from all that has been written, success seems to depend on the type of anuria for which the decapsulation is done.

In attempting to discover how improvement can occur, investigators found there was a difference in the amount of urine excreted if the decapsulated kidney was made diuretic by saline infusions, etc. Some secreted more during diuresis, *i.e.*, as a response to increased demand, others less (46). The blood flow, even after corrosive sublimate poisoning, was always better (47). Ferrarin (48) could obtain no success from this operation in experimental uranium poisoning. But very few deductions for decapsulation may be drawn from these experiments, because we do not yet know with certainty what produces the anuria in acute nephritis. If there is actually vascular spasm, it is necessary to assume with Volhard (33), that decapsulation forced this spasm to relax, through injury of the ganglion cells of the hilus.

But we also know of good results from nephrotomy in anuric conditions (49). Conversely, it has been assumed, furthermore, that the kidney of acute nephritis required expansion on account of vascular congestion and edema, but was prevented by the unyielding capsule. This would lead to compression of the capillaries—"glaucoma" of the kidney—and the often described "bulging," which is observed during decapsulation, seems to support this view.

These conditions are by no means clear. The most necessary data, are accurate observations on patients. Only really pronounced cases will prove anything, because experience shows that such anurias often disappear spontaneously.

Decapsulation was advised not only for acute anuria, but also for chronic nephritis (Edebohl (50)). The conception on which he built his theory was that after decapsulation, not only would collateral circulation develop, sufficient to remove toxins and other substances noxious to the kidneys, but this improved vascularization would help in the healing of the inflammation. A disproportionately large number of investigators has attempted to demonstrate whether this collateral circulation is actually evolved from the renal cortex (51). Its extent was observed either in injection preparations (partly by *x*-ray pictures), or by observing if decapsulation is completely or partially capable of preventing the circulatory disturbances which follow ligation of either the renal artery or the renal vein. In a number of cases, the kidney was imbedded in omentum to assist in the formation of this circulation (Bakes). A new capsule formed very quickly, probably starting from the torn vessels. A certain, although superficial collateral circulation seemed to form when the kidney was enveloped in omentum, but that this became abundant enough to permit the ligation of the renal artery without producing the usual total necrosis, as has been



reported by some writers (Parlavecchio, Lobe, Katzenstein), is only an experimental error. In the dog, as Liek has shown, there are, normally, so many collaterals and side-branches that the renal artery may be ligated without decapsulation. Thus the assumption that this procedure brings about circulatory improvement by collaterals is purely hypothetical, since what follows is merely a process of cicatrization on the renal surface. Furthermore, Bright's disease is not always a process due to deficient blood supply, but may be primarily cell degeneration, with secondary vascular atrophy. Finally, the whole conception of the elimination of toxins is equally vague. Taken all in all, the attitude of aloofness of the majority of surgeons in relation to this operation is quite intelligible (52), (49) and the good results reported by Edebohl himself, have been destructively criticized by a number of authors (53). In many cases, Rovsing's objection is justified; they were not cases of Bright's disease at all; in other cases, the reports were made after only a very short time had elapsed. How the good results in the remaining cases are to be explained, cannot be decided at present. According to Zondek (54), the capsular vessels have valves to take care of the great physiological blood pressure fluctuations in the kidney, thus decapsulation robs the kidney of a very essential protective apparatus.

But the decapsulation experiments have unearthed an important fact, *viz.*, that the renal artery itself is not an end artery but that anastomoses and collaterals are especially well developed in some species of animals. That, in the dog, for instance, is so complete, that even bilateral ligation of the renal arteries does not cause death. The artery divides at its entrance to the kidney into an anterior and a posterior branch, and as Zondek's (55) investigations have shown, the level at which these two vessels divide does not lie in the same plane of section, but 0.5 cm. behind. For other details concerning the renal vascularization, Albarann (56) may be consulted; moreover, the transplantation experiments show that the kidney can support interruption of its circulation for some time (57), (10). Compression can be withstood, without causing clinical symptoms, for 10 or 20 minutes (58). But that compression of the renal vessels for but a short time may lead to albuminuria, is shown by the appearance of this substance in the urine after palpation (Schreiber), a fact of diagnostic importance, if the origin of a tumor in this region is not clear from palpation (59). Cohn (60) studied this matter experimentally.

Ritter (61) recently advised ligation of the renal veins in the treatment of bilateral tuberculosis of the kidneys. Necrosis does not usually result, but there is always a tremendous lasting hyperemia. Buchwald and Litteu, Weissgerber and Perls (62) subjected this proposition to animal experimentation. Small hemorrhages appear in the renal parenchyma,

and gradually a contraction of the whole organ takes place with hypertrophy of the other kidney; the renal function, however, remains permanently unimpaired in spite of the ligation. Consequently, there must be collaterals, although restricted in numbers. But whether ligation of the veins can exert a curative influence on tuberculosis will be shown only by further experience, and comparisons of the favorable influence of atrophic processes in the lung in pulmonary tuberculosis are not possible without reservations. The experiments of Isobe show that ligation of renal veins is by no means a harmless procedure; for he lost all the animals in which he performed a unilateral nephrectomy and then tied off the vein of the other kidney (63).

The *effect of venesection* in uremia is also difficult to explain. Once again, a true uremia must be differentiated from so-called pseudo-uremic symptoms. The experiments of Becker have shown that venesection does not constitute a detoxifying process; on the contrary, the amount of retained nitrogen in the blood as well as that in the tissues, increases. The statement that is frequently made, *viz.*, that dilution of the toxins and washing out of the tissues take place, is, therefore, incorrect. In fact, venesection does not help in true chronic uremia, but its influence on the headaches, spasms and convulsions is often remarkable, that is, on those symptoms which are summed up as pseudo-uremic, as stated above. In this condition, the beneficial influence of venesection is expected primarily from its action on the circulation. In healthy individuals, the blood pressure remains practically normal after the removal of small or medium amounts of blood, because the vessels contract and a current is quickly established from the tissues into the blood; in arteriosclerotic and uremic patients, considerable lowering of blood pressure is observed, because the regulative contractibility of the smaller vessels is impaired (64). Whether this decreased blood pressure, and the lowering of venous tension, which is also demonstrable, have any influence on cerebral circulation or in any other way, is still in hypothetical regions.

The question of whether disease or injury of one kidney is detrimental to the function of the other kidney, has often been raised, *i.e.*, whether there are *relations between the two kidneys*, somewhat similar to those between the two eyes.

Isobe (65) investigated this problem by ligating the vessels of one kidney, either the vein alone, or both artery and vein; and examining the other after some weeks had elapsed. He always found parenchymatous changes in one after severe injury to the other, and he correlates these changes with absorption of decomposition products formed by the injured kidney (nephrolins (45)).

Hyde (66), after displacing both kidneys of rabbits under the skin of the back, found no trouble in the remaining kidney after the removal of the other, but squeezing one produced oliguria and death. Fiori (67) reports experiments in which ligation of one ureter, was followed by lesions in the other kidney. Clinically, cases are known in unilateral renal tuberculosis, in which albuminuria from the sound kidney ceased as soon as the tuberculous kidney was removed (Kummell a. o.). Meaugedis (68) gives a similar report in unilateral renal calculus.

But how much of a "specific" correlation there is between the kidneys in all these investigations and observations is not certain. As is well known, they respond with nephritic symptoms to all kinds of diseases and injuries to the rest of the body, and it is not surprising when one kidney is removed, or its function impaired, that the remaining one should be affected in a greater or less degree. An increased sensitivity of one kidney to injuries affecting the other, cannot be deduced from the findings in the experiments described, but the hint that in unilateral renal disease the other kidney is also in grave danger, is of great practical importance.

Human kidneys occupy such exceptionally protected positions under normal conditions that an explanation of how *blunt injury* can reach them, causes some difficulties. As experiments of Maas (69) have shown, it is easy to grasp the kidney of a rabbit between the abdomen and the back and to crush it between the fingers. But in man such a mechanism cannot operate, because the force required would have to be so powerful, not only because of the distance between the abdominal wall and the back, but also because of the tension of the abdominal walls, and injury to the intestines could not be avoided. Furthermore, as Kuster (70) points out, renal tears running diagonally into the pelvis, as is usually the case, cannot be due to direct crushing. They can only result from hydraulic pressure, and in suitable experiments, Kuster could show that kidney tears similar to those observed clinically, can be obtained if the renal veins in a cadaver are ligated, the kidney filled with water through the artery, and a blow struck against it. This is especially effective by reason of the movable lowest ribs. The direct consequence in patients is first, hemorrhage, and then cessation of renal activity—anuria. In the traumatized kidney, it is probably the injury to the vessels which causes anuria; but the other intact kidney also fails at times. This is spoken of as "reflex anuria," which will be discussed later.

*The healing of renal wounds* of all types has been studied many times both experimentally, and in man (71), (69). It was necessary to show first, how wounds of the kidney heal, and what histological processes may be observed, and secondly, whether a true regeneration of the glandular



elements takes place. At the same time data accumulated, which showed how much kidney tissue could be removed without endangering the life of the animal.

The kidney heals readily. As in every wound, at first we find necrosis of the tissue adjacent to the surface of the cut; the convoluted tubules disintegrate in a remarkably short time, but the glomeruli are more resistant. The lesion fills with serum and fibrin (72) and after even a few days, the tear is filled with a delicate, highly cellular connective tissue. There is growth of the epithelium, but functioning gland tubules are not found; the growth is somewhat irregular and the tubules are merely solid buds of epithelial cells.

The connective tissue soon contracts, so that according to Windboltz (73) only a small scar remains after nephrotomy. But Langemak and Hermann (74) obtained larger lesions after longitudinal section of the kidney, and they advise the less injurious transverse section. This difference in results depends on the vascular architecture, so that Simmonds found a scar only of the thickness of the back of a knife two years after nephrotomy (75). The remaining part of the kidney enlarges, similarly to the hypertrophy of the other kidney after unilateral nephrectomy.

Enderlen (76) has studied the histological changes in the remaining kidney after the latter operation. It is now practically proven by the experiments of Barth and Wolf, that enlargement is due only to hypertrophy, and not to the formation of new renal substance. New growth of functioning kidney tissue does not take place, especially is there no new formation of glomeruli, as was formerly asserted.

*The ability of the remaining kidney tissue to function* after experimental operative interference does not, generally speaking, depend on the amount of tissue removed, for after the removal of one kidney, portions of the other amounting to one-third to one-half of its original weight may be sufficient to prevent any impairment of function as shown by the ordinary tests. On the other hand, animals have died of uremia, when much less kidney substance was removed, but at short intervals. Therefore, kidney function does not depend merely on the anatomical lesion. But in spite of this, it must be concluded from the polyuria in cases of kidney shrinking (see later), that operative reduction of kidney mass is followed by diminished function, even though we may not be able to demonstrate it by the ordinary methods. The hypertrophied kidney after extirpation of one organ or after injury, is especially liable to functional changes in the beginning, as observed by Wossidlo (77). He showed that the epithelium is increasingly permeable after carmine ingestion, so that the filtering power of such a kidney might fail in a short time when extraordinary



burdens are laid upon it. The normal permeability is reestablished only gradually.

Even though the proper functioning of the *adrenals* is essential and a regular undisturbed excretion of adrenalin is necessary for surgical successes, nevertheless, they are seldom interfered with operatively. The few experiments which have been done from the surgical point of view, have been confined to the possibility of transplantation or to the demonstration of the changes the glands undergo after operations in their vicinity, especially after kidney operation.

Suprarenal glands were either transplanted at a distance from their original site, or imbedded in the kidney substance with or without pedicles (78). It was hoped that hypernephromata would arise from these transplants, but all the experiments failed. Indeed it is very questionable whether the so-called Grawitz hypernephroma has anything in common with misplaced adrenal rests; possibly it is a tumor, originating from the renal tubules themselves (79).

Nakahara (80) found changes in the chromaffin cells of the adrenal medulla after operations on the kidney, but they were so variable that they can be considered purely a result of contusion, and quite unrelated to influences from the kidney. Since one of the adrenals can be removed without endangering the organism, no special precautions are required in kidney operations.

Of much greater pathological physiological interest than severe traumata, are the disturbances frequently considered the result of very slight "trauma" and grouped under the name of "*orthostatic albuminuria*" (81). By this is understood, a disease picture, in which periodically, with no subjective knowledge on the part of the patient, a considerable amount of albumen is excreted. Usually it is preceded by unusual physical exertion; but it is often found after merely arising from bed and it quickly disappears if the patient is kept in a prone position. But Posner, Senator (82) a.o., have shown by their investigations, first, that the urine of every normal individual shows faint traces of albumen with especially sensitive reagents, and secondly, if a normal individual engages in exceptional physical labor, this output of albumen is increased to such an extent that it can be demonstrated by the boiling method. Such studies have been made after all sorts of athletic contests. But the albumen excreted never approaches the quantity found in this so-called orthostatic albuminuria, in which it appears after "physical exertion," which like merely arising from bed, does not deserve this name. Therefore, we must assume that there is a special inferiority of the kidneys, and an exceptionally marked permeability to albumen in such individuals. The cause for the albuminuria must reside in the patient himself, while the different external causes

("trauma") must be regarded merely as accessory factors. This renal inferiority may be a temporary condition, only present in adolescence and disappearing later.

From many studies of the external causes, a large amount of interesting data is available which cannot be correlated; for example, there were patients who showed no albumen or only a slight trace after the fatigue incurred by a mountain trip, but it reappeared after much less trying exertions. In these cases it cannot be the degree, but the type of physical activity which is responsible. According to Jehle, it is the exercise in which patients bend their lumbar spinal column sharply to the lordosis position (83). Such patients usually have a natural tendency toward lordosis and Jehle speaks of a "*lordotic albuminuria*." But this can only be considered, after the previous statements, an external cause in a predisposed individual. There are youthful patients with quite marked lordosis, *e.g.*, in juvenile muscular atrophy, who show no pathological elimination of albumen (84). Therefore, lordosis with orthostatic albuminuria is probably to be considered a sign of tissue weakness. Jehle points out that to assume the upright position from the ordinary quadruped position must at first have necessitated a lordosis, as is seen now in anthropoid apes. But in man, with a muscular development suitable to the upright position, lordosis of the lumbar spine has been diminished. In addition to albuminuria, such patients show a cylindruria, and a diminished secretion when albumen appears. To this are added certain disturbances in the chemical composition.

At present, it is thought that lordosis produces an effect on the kidney through circulatory disturbances. It is not clear whether other factors also play a role—the innervation for instance. At any rate, albuminuria ceases, even in an upright position, if a corset corrects the lordosis. Bunge (85) has recently shown that mechanical pressure on the normal kidney will cause albuminuria and he has suggested a special position for renal operations.

*Massive hemorrhage* into the bed of the kidney must also be considered one of the lesser traumatic injuries (86). It must not be confused with injury caused by a blow, and while Ricker (87) obtained hemorrhage in the capsular region after ligation of the renal veins of animals, such hemorrhages were only occasionally observed in the kidney itself. Therefore, congestion must be a necessary factor in producing this peculiar symptom. With Ricker we can easily imagine, that the sudden filling of a hydro-nephrotic sac, or change of position, as may occur in a floating kidney, may lead to stasis in the renal vein. But stasis alone does not explain this disease complex; even experimental hemorrhage from ligation of the renal vein is insufficient. Something else must be added to account for

the permeability or increased hemorrhagic tendency of the vessels, and present data seems to indicate that these massive hemorrhages into the renal bed have developed mostly in those kidneys altered by chronic inflammatory changes. Possibly they are the cause of the tendency, but in seeking its source, we encounter the difficulty of determining whether it comes from the kidney itself, or from a vessel outside the kidney. To assume a capillary bleeding is somewhat unsatisfactory, considering its amount and its sudden onset.

Normally *the fixation of the kidney* is not rigid but only relatively so. Although, according to anatomists, a connective tissue thickening designated as renal fascia gives support to the kidneys, it is not these bands, but the support supplied by the mutual interaction of the different tissues of the body, which is the deciding factor in renal fixation. Tissue tonus and its changes are responsible for the positions assumed by the abdominal organs. No one has a better opportunity of observing the importance of this tissue tension and tissue firmness than the surgeon, who must daily take it into account in his operations. Even the beginner knows the "poor" fascia in hernia for which no explanation can be found as a local condition, and which can be correlated only by the conception, at present very hazy, of some general physical condition.

We have touched upon all these things in discussing enteroptosis including its relation to the physical type (*habitus asthenicus*, Stiller). It must be remembered that *ptosis of the kidney* almost never occurs alone, but that it is only one of the symptoms of general enteroptosis. Of course, the disturbances caused by such a kidney may predominate to such a degree that the ptosis of other viscera is entirely overlooked. For this reason, it is often forgotten in the chapter on floating kidney that it is only one symptom of a general body condition which is not necessarily congenital. Sudden loss of weight (88), pregnancy, etc., may lead to ptosis, just as "disposition," as was mentioned above in discussing maternal enteroptosis.

Nevertheless, mechanical factors force themselves on our attention, because, as Kuster points out, floating kidney occurs mostly in women and then chiefly on the right side (89). Direct injuries of the kidney region must be named first among "mechanical influences," but in addition, the more chronic injuries may also be considered, *e.g.*, riding in a side saddle. According to investigations of v. Fisher Benzon (90), (Heller), tight lacing causes lateral displacement of the right kidney from pressure transmitted by the liver. The much quoted anatomical investigations of Wolkoff and Delitzin (91) offer certain supporting points in explanation of the facts that the right kidney is more often floating than the left; and that it is more common in women. These investigators showed with plaster casts



that the kidney beds resemble niches, and that these niches are deep and funnel shaped in man, while in woman they are flatter and cylindrical, and in floating kidney this flattening increases. Furthermore, they found the right niche more shallow than the left. At present, the indication for operative fixation in renal ptosis, depends chiefly on the temperament of the surgeon in question. This is shown by the fact that some busy surgeons do not operate for floating kidney for years, while others in the same length of time see fit to operate hundreds of cases. This statement also shows how little is known of the whole question. The fact remains that few operations are performed at present, which means that the results are not very brilliant. In other words, it has been recognized that a large part of the disturbance blamed on the floating kidney (as backache, etc.) is not due to this condition, but is a sign of the peculiar general nervous constitution of such individuals. But sudden and very severe attacks of pain combined with collapse, meteorism, rigidity of the abdominal walls, in fact all the symptoms suggestive of renal colic, are sometimes encountered. Since Dietl's (92) time, this is spoken of as *renal incarceration*, and although it is very questionable whether the cases seen by Dietl were not acute cholecystitis, there is no doubt that such attacks of pain occur from kidney conditions. For the present, it is not certain how they are to be explained, and possibly several factors contribute. Thus far there is hardly any operative experience recorded during the acute attacks, but Borzeky (93) reports a case of torsion of the kidney pedicle. The attack of pain in this case was produced by the circulatory disturbance and this is a hypothesis which plays a great role in the explanation of "renal incarceration" since Landau (88) emphasized it. A sudden kinking of the renal pedicle is supposed to take place and the venous outflow is obstructed and the result is a swelling of the kidney which can be palpated during the attack. Atrophy and contraction have also been accepted as the late results of such circulatory disturbances, and these have occasionally been found at autopsies of patients with old floating kidney. Other writers (94) believe that the pains must be interpreted as hydronephrotic, since it is well known that hydronephroses can occasion such pain. We will speak later of the conditions resulting from floating kidney.

The tissue surrounding the kidney has abundant nerves originating from the lumbar spinal cord, and thus every pull and position change, or stretching of the pelvis, must be painful (15). But it has not been decided whether the pelvis has its own sensory sympathetic fibres (see above). In many abdominal affections we often find an incongruity between the subjective pains and the actual findings, and it is, therefore, not justifiable to expect a pronounced anatomical condition in so-called



"renal incarceration." Israel considers a pull on the renal attachment and on the perirenal nerves quite sufficient to explain the pain. Conversely, Riedel in his explanation of all the disturbances in floating kidney, saw extensive adhesions, but only during laparotomy. We must admit that it is impossible to judge at present how the pain is produced. It may be in the kidney itself, for such attacks have been known to occur in nephritis, and floating kidneys showing nephritic changes have often been found, but the details are unknown. Since slight trauma (palpation) affects the kidney, producing albumen excretion (see above); and since this trauma is in a sense repeated innumerable times in floating kidney, this may be supposed to lead finally to nephritis. But then we should only obtain a unilateral chronic parenchymatous nephritis, and the question of whether it actually is unilateral in such cases, is still very problematical (45).

As stated, a number of writers believe that the acute painful attacks are related to stasis of urine in the pelvis, from kinks of the ureter where it emerges from the pelvis. Then in the course of the disease, or after repetition of this sudden kinking, enlargement of the pelvis results; *i.e.*, an *hydronephrosis*. In experiments made by Tuffier and Hildebrand and Haga (95), these changes have been followed in animals by producing a hydronephrosis after the establishment of an artificial floating kidney and ureteral kinking.

It is not difficult to understand that mechanical factors play such an important part in the development of hydronephrosis. Abnormal vascularization, renal incarceration, scar tissue within the ureters, are all known causes. A very extensive pertinent literature has been built up, and experimental studies dealing with the results of ureteral ligation are also available in large numbers (96). All the mechanical obstructions affect the ureter itself, from its point of emergence from the pelvis. But hydronephrosis also occurs in hypertrophy of the prostate, phimosis, hypospadias, etc.; *i.e.*, in cases in which the obstruction makes it difficult to empty the bladder, and in which a backflow of urine through the ureters into the pelvis might take place. Numerous investigations and observations have shown that the oblique entrance of the ureter into the bladder is no absolute protection against backflow (97). Normally, the ureteral orifice opens periodically, probably under the influence of ganglion cells situated within its walls. But if, for instance, the filled bladder contracts at the moment when the ureter opens, urine may flow backward and reach the pelvis, as Levin and Goldschmidt showed by manual pressure on the bladder. It is obvious that this organ contracts more often, and more suddenly in inflammations and thus more frequent opportunity is given for this backflow. If the normal ureteral openings are no absolute pro-

tection against backflow, it follows that the pathological orifices are still less so, and by cystoscopic examinations, they are found wide open after the passage of calculi, in tuberculosis, etc., but even if the obstruction is more peripheral, *e.g.*, in hypertrophy of the prostate, they are also found gaping. In such cases it must be assumed that the ganglion cells have finally failed. If the ureteral orifice is open, the backflow of urine is unimpeded, and hydronephrosis is the inevitable result. After the injection of collargol into the bladder, *x*-ray examinations show both ureters and renal pelvis filled with the substance (Rost (97)).

Still other factors favoring the development of hydronephrosis are disturbances in the activity of the ureter itself, exclusive of its orifice. Peristaltic waves normally travel at irregular intervals from the pelvis to the bladder, and are controlled by numerous ganglion cells in the walls of the ureters (98). If the ureter is cut through transversely, the peristaltic waves go only as far as the incision (99) and for this reason the removal and replacement of a section of the ureter is unsuccessful. Hydronephrosis develops in all such animals (100). Similarly it is very rare for a peristaltic wave to pass over a constriction. Furthermore, such disturbances in the ureteral motility can be produced by loosening it over extensive areas (101), for when its vessels and nerves are stripped, the ureter ceases to move. The result is hydronephrosis, and if bacteria enter the bladder, pyonephrosis. Such extensive loosening is done if the ureters are conducted through the skin of the loin after total extirpation of the bladder, when infection of the pelvis always follows, but in man it develops after a longer interval than in animals (102). On the other hand, the investigations of Lorin (103) have shown that the ureter which has been cut through, without having been loosened, as in nephrectomy, retains its motility for two to three years after which it becomes obliterated. In the experiments of Aksne the stump of the ureter showed antiperistaltic waves. As can be seen in the cystoscopic field, the orifice also moves for a long time after cutting through the ureter above.

Ureteral function can also be disturbed as a result of inflammation alone. Thus Primbo (104) obtained inhibition of motility in the ureter of guinea pigs by applying bacillus coli toxin to it.

The consequence of such urinary retention in all such cases is dilatation of the pelvis.

Polyuria caused by urinary retention, has been discussed. If the ureter is ligated, as may happen in gynecological operations, distention of the renal pelvis ensues with a gradually increasing pressure atrophy of the renal parenchyma. The glomeruli are preserved longest (105). But ureteral ligation for a short time is more interesting to the surgeon. The investigations of Rautenberg (96) show that injuries caused in this

way are quite lasting, for progressive parenchymatous atrophy developed after occlusion of the ureter for 14 days and more. If the obstruction was removed the parenchyma recovered slowly, and extensive regenerative changes appeared, leading to the formation of apparently perfectly normal urinary tubules. Scott (106) confirmed this result. But such regenerated tissue is not viable, it slowly breaks down, and the atrophy continuing in spite of the regenerative interruption, leads gradually to death. It is shown clinically by permanent albuminuria. The experiments of Boetzel (107), in which he stained rabbits intravitaly after ureteral ligation, and later observed the distribution of the granules, give an idea of the changes in the cells.

In incomplete obstruction, the dilatation of the pelvis is less marked, and its variability has been recognized only since the application of collargol injections, with subsequent *x*-ray observation (108).

In the past, the interest of investigators was attracted to the result of injection of fluid into the pelvis by the subsequent finding of air embolism; although Marcus (109) afterwards showed in reinvestigations, that it occurred only if small tears were made in the mucosa. Recently, all kinds of accidents have happened during the injection of collargol (110) and the question of whether it causes injuries, was again raised (Wossidlo (111)). It was shown that under great pressure, collargol not only penetrates into the lymph spaces and renal tubules, and thus injures the kidney, but may directly enter the circulation through injured vessels. Disturbances which must be explained similarly are occasionally seen in lithotripsy, when fluid mixed with air is driven into the bladder from the aspirator under too great a pressure.

The degree of hydronephrosis depends, of course, on the resistance offered to the outflow of urine. In minor obstruction, *e.g.*, phimosis or hypospadias, decades may pass before renal insufficiency appears. In such cases the pelvis may be found but little distended, and renal insufficiency is probably a result of the parenchymatous atrophy.

To what degree injuries, especially progressive ones, are caused by milder forms of hydronephrosis is not easily determined, since the latter could be diagnosed with certainty only after the introduction of pyelography. At any rate, the relation of hydronephrosis to degenerative nephritic processes is most important, because the dangers of hydronephrosis, and the often accompanying pyelitis are frequently underestimated (112) and thus far, have received very little direct study. It is hardly justifiable to assume that dilatation of the pelvis in man is always accompanied by progressive renal degeneration, as it is in animals, because an enlarged renal pelvis is found in 30 per cent. of all pregnant women, according to



data from the autopsy records of Hirsch (113). Certainly not that number of women have progressive renal disease.

Since stagnation of urine favors the development of bacteria, a hydro-nephrosis may readily become a *pyonephrosis*, and as we have just seen, stagnation of urine due to toxic paralysis of the ureters is always increased by inflammation. Thus another vicious circle may be established. There are three ways by which infectious organisms may reach the pelvis, and probably all are used; by way of the circulation, through the lymph channels, and from the bladder through the ureters (114). Ordinarily the route can be recognized only on the merits of the particular case. In advanced cases in which the whole kidney is destroyed, it is probably impossible to decide by what route the infection entered.

The type due to vascular infection shows the multiple abscesses of pyæmia, but when the disease is complicated by a toxic nephritis, only the presence of pyogenic organisms (usually cocci) will prove its existence (115). These multiple abscesses are very easily and consistently obtained after the injection of bacteria into the circulation and Brewer produced them unilaterally if he traumatized one kidney previous to the injection (116). In man, very large unilateral abscesses occur in greatly swollen kidneys where a preceding suppurative inflammation in some other situation points to embolic infection. Why a multiple dissemination of small abscesses should occur in one case and a single large abscess in another, is not known. Since small abscesses appear oftener in severe septicemia and single abscesses occur more often in furunculosis, infected wounds, etc., the number of bacteria carried and their virulence must play a part. Koch (117) who took virulence into consideration, found chiefly medullary foci with almost intact cortex after injecting weakened cultures; after injecting virulent organisms, more of the cortical foci were seen. Hematogenous unilateral suppuration can also be obtained experimentally (118), (117).

A very important surgical question in such suppurative nephritis is whether the pelvis is involved or not; a hematogenous abscess may discharge into the pelvis, and lead to pyelitis, but such infections are usually not severe (119). But the reverse may happen, *i.e.*, the pelvis is first infected and by ascending, the process infects the kidney. Consequently, there may be a smooth transition from the mildest pyelitis to the most severe pyonephrosis. This latter condition is one of the commonest of surgical renal affections, and the organism is found to be *bacillus coli* in most of the cases.

The route by which the infection reaches the pelvis has provided a field for speculation and experimentation. In cases in which severe cystitis is coexistent, as in the pyelitis of children (120), and in cases with difficult urination, as in pregnancy or hypertrophy of the prostate, there is



dilatation of the pelvis, open orifices of the ureters and backflow of urine, so that it is probably quite natural to think of an ascending infection. Even if we assume that the pelvis is secondarily involved from a cystitis, nothing can be said as yet in regard to the route by which ascending infection took place. It is not without reason that doubts have again and again been expressed as to the apparently logical assumption, *viz.*; that bacteria are carried through the ureters to the pelvis, infecting it thus. The question is not so much how bacteria may reach the pelvis by this route, but why the few organisms which happened to be suspended in the urine could give rise to inflammation of the mucosa of the pelvis, when, as stated above, a renal abscess, discharging myriads into the pelvis, affects it only slightly. But an infection may also be carried from the bladder to the pelvis by the lymph route. Sakata and Bauereisen (121) have described such lymph channels surrounding the ureter, and Sugemura (122) demonstrated that the lymph channels constantly showed inflammatory changes in cystitis. Lever Stewart (123) transplanted the ureters into the bowel and then found extensive infection of the blood and lymph vessels surrounding the ureters.

Why is it that the colon bacillus is the usual infective agent in the urinary tracts, while other organisms are rarely found in this group of inflammations? It cannot be an infection entering from without; and unquestionably the most logical idea is that an individual infects his urinary tract with his own colon bacilli; and this is now the generally recognized view.

These bacteria can reach the urethra from the anus, and then ascend to the bladder. This form is probably the principal one in female children, and as proof of the correctness of this supposition, nearly 90 per cent. of the children affected with pyelo-cystitis are girls (120). This form of infection is frequently assumed to occur even in adult female patients, but this seems somewhat forced.

But bacteria confined to the intestinal tract can reach the urinary tract in other ways than through the urethra. First, it must be demonstrated that they are able to penetrate the bowel walls under normal conditions. This has been discussed on page 240. In the experiments quoted there, the essential point was to demonstrate whether bacteria could reach the peritoneum through the walls of the bowel; here the question is to discover if intestinal bacteria can enter the lymph channels of the intestines. The result of these different investigations and the present viewpoint are found in the works of Selter, Conradi, Rogoczinsky, Hornemann, Nocard, Posner and Cohn (124), *a.o.*

Accordingly, it may be accepted that colon bacilli are almost always present in the mesenteric lymph nodes, and from these same investigations

it may be said that even in freshly butchered animals, bacteria are found in all the organs. This fact is of wide interest to the surgeon, because it is often necessary to face the question in the medico-legal side of accident cases, whether a given limb was, or might have been infected through some injury. Often it is necessary to assume that bacteria circulate in the blood or remain in organs from which they may easily enter the circulation at any time. As has been stated, this assumption is supported by the experiments described.

The anatomical investigations of Francke (114) give information concerning the route by which colon bacilli reach the lymph nodes from the colon, and from there to the kidney. He could show, by Gerota's method, that lymph channels run from the caecum to the right kidney, and similar channels go from the descending colon and the sigmoid to the left kidney. Since the permeability of the bowel wall is increased considerably by even slight catarrh, such a process may be an occasional causative factor in producing an infection of the pelvis of the ureter.

The reports of Wasserthal, Epstein, Roubitschek (125), *a. o.* show that the relation of intestinal diseases to renal diseases is often still more complex, as *e.g.*, when albumen and cylindroids appear in the urine after the constipation produced by opium. Writers consider this due to reflex congestion in the renal region. It is not known whether bacteria appear in the urine in such albuminurias, but Brunn (126) demonstrated focal necrosis in the kidney in cases of ileus, and could also confirm this finding experimentally. Aseptic abdominal operations *per se* were followed by no such necroses, but in cases of peritonitis they could frequently be found.

Colon bacilli can also enter the urinary tract from the rectum through the tissue situated between it and the bladder, but this form of infection is rare, at least a correlated cystitis is found but seldom even with perianal abscesses. Without doubt, such bacterial invasion is more frequent in animal experimentation, although under conditions rarely observed in man. Thus Wreden (127) obtained cystitis in the rabbit after injuring the upper rectum and Faltui (128) who repeated these experiments, obtained it only if he injured the bladder also. Here too belong the investigations of Posner and Lewin (129) who proceeded from another viewpoint, but ligated the anus in rabbits and then obtained cystitis and pyonephrosis. The animals succumbed quickly. Marcus (130) who imitated these experiments, thinks that in those of Posner, the escape of bacteria from the bowel was only possible on account of the extensive injury of the surrounding tissue, and that the bladder and renal affections were due to Posner's experimental methods. If the bacteria once reach the lymph nodes, it is not difficult to understand how they enter the circulation.

It is not certain whether a *B. coli* bacteremia is present in pyelocystitis. A true coli-septicæmia is quite rare; and it could only mean a local or quickly passing infection of the blood. Probably bacteria which have penetrated the kidney substance from the blood route may pass through (see Orth's nephritis papillaris bacterica (131), (117)).

In what manner do bacteria reach the kidney substance from the renal pelvis, in other words, how does a pyonephrosis develop from a pyelitis (132)? After injecting bacteria into the renal pelvis, a suppurative infection of the kidney tissue can be produced only when complete retention and active congestion is caused by ligation of the ureter. A. Muller (133) has critically reviewed the different experiments in this direction, and amplified them by his own pathological anatomical investigations. He concludes that in the vast majority of cases, the extension of pelvic inflammation to the renal parenchyma occurs through the lymph channels, *i.e.*, in the tissue surrounding the urinary tubules. It is only under exceptional experimental conditions, seldom found clinically (*e.g.*, ligation of the ureter), that an ascending inflammation in the urinary tubules occurs.

In speaking of hematogenous infections of the kidney, it must also be mentioned, that conversely, bacteria easily reach the circulation from the urinary tract. Thus Bertelsmann and Man (134) demonstrated that in the so-called catheter-fever, *i.e.*, the often observed rigor and fever following immediately after catheterization, bacteria are found in the blood with great regularity.

Suppurative inflammation of the kidney may lead to an infection of the perirenal tissue (*paranephric abscess*), since in this region blood and lymph vessels are in the closest relationship to the kidney (119), (135). The perirenal tissue, undoubtedly, has a special tendency toward suppuration, but it is not very certain why this should be. Inflammatory processes from the lung may localize here, as well as infections through hematogenous sources. Schnitzler has obtained such metastatic perinephritis in the rabbit by the injection of staphylococci into the circulation and later contusion of the renal region. But it must be decided in each individual case by which of these routes the perirenal tissue was infected. At present the general tendency (136), is to assume that in the majority of cases, small pus foci were situated under the kidney capsule from which the inflammation spreads. The presence of such foci is deduced from the finding of isolated leucocytes in the urine. It is now a well known fact that in numerous infectious diseases, bacteria are discharged in the urine (bacteriuria) and this is of especial importance in typhoid prophylaxis.

As in suppurating renal inflammations, the question of whether



*tuberculosis* ascended from the bladder or entered by way of the blood or lymph channels, was discussed pro and con for many years (137), (26). Pathological anatomy could not decide the question because at autopsy only end results were seen in which the bladder is always much changed. Clinical observations, especially by means of cystoscopy and operation, showed whether renal tuberculosis can exist without tuberculosis of the urinary bladder. Of clinical investigative methods the most certain proof of renal tuberculosis would seem to be the finding of tubercle bacilli in the urine. But urinary examinations made by Foulteron and Hillier, Rolly, Jousset, Kielleuthner (138) have shown that tubercle bacilli are excreted in the urine in severe phthisis, when no tuberculous foci can be found in the kidneys at autopsy. Kielleuthner produced proof that the tubercle bacilli did not enter the urine from the testes in such cases, but that they actually pass through the kidneys without forming colonies. Thus the presence of tubercle bacilli in the kidney does not constitute renal tuberculosis; something else must be added to encourage the bacteria to settle in the renal parenchyma and to destroy it. In the first instance, it is natural to think of traumatic causes in the widest sense of the word, and correlated experiments were made by a number of workers (139). The kidneys were contused, or injured by means of temporary ligation of the vessels, and tubercle bacilli were then injected into the ear vein of the animal with the result that the injured kidney showed more abundant tubercles than the healthy one. But these lesions were different in type and localization than those seen in human renal tuberculosis, as will be discussed later. Statistics show (140) that a corresponding trauma can be traced in but few human cases. For this reason search was made for all possible diseases or renal lesions which might favor this infection, such as pyelitis, hydronephrosis, renal calculi, floating kidney, and malformations. Generally speaking, these accidental findings are of no value in regard to its pathogenesis, but under certain circumstances, and not as a rule, injuries may favor infection. In animals, a kidney, made artificially hydronephrotic, becomes more easily tuberculous than an uninjured organ, which is due, according to Meinertz, to the venous stasis usually present (141). This view, that circulatory changes, especially congestion, active or passive, may favor the growth of tubercle bacilli in some way in an organ, will be repeatedly encountered, *e.g.*, in tuberculous orchitis.

There is a difference between experimental tuberculosis, and that found in man, insofar as in the animals there is only a miliary dissemination of the tubercles, and that chiefly in the cortex, while in human tuberculosis, the infection begins with isolated tubercles in the medulla. Because of this primary lesion in the medulla, it was assumed at first that renal tuberculosis is an ascending infection, *i.e.*, from the bladder. But the



experiments of Pels Leusden (142) have shown that the injection into the renal artery of a few, mildly virulent tubercle bacilli suspended in oil, gives rise to unilateral tuberculous foci in the medulla. Thus we may have a distribution of tubercle bacilli in a manner similar to that of pyogenic organisms (117). It also seems to show that unilateral renal tuberculosis in man and its localization in the medulla does not depend on single bacilli, but on tissue fragments containing tubercle bacilli which enter the circulation.

The complete acceptance of a hematogenous origin which is at present practically general, meets nevertheless with other difficulties. In unilateral involvement, the other kidney is often infected later, while no new tuberculous foci appear elsewhere in the body. Why does not bone infection, etc. occur? French writers (Albarran (143) and Cathelin) believe that transmission occurs through a blood vessel which they have demonstrated passing from one kidney to the other, but it is easier to think of the lymphatics. Tendeloo (144) is of the opinion, on the basis of some autopsies in which he found pulmonary tuberculosis with pleural and diaphragmatic adhesions on the same side and also tuberculosis of lymph nodes and kidney, that renal tuberculosis is altogether mostly lymphogenous, an opinion which has found but few followers.

Furthermore, it has been assumed that the kidneys of patients who have acquired tuberculous nephritis always were especially susceptible to this infection. This is an opinion very difficult to prove at present. In discussing osteomyelitis we will again touch upon this question and it should not be ignored. Many cases of this disease give the impression that the bacteria have an affinity for certain tissues of the body, or conversely, that the tissue shows a special predisposition to the particular infection. Israel, among others (26), also thinks that tubercle bacilli grown in the kidney have a special affinity for renal tissue and that, therefore, the other kidney is more easily infected.

Tuberculous infection of the bladder is secondary to the kidney, and for this reason, the first ulcerations are usually at the ureteral orifice of the diseased kidney. Since they are very persistent even though the diseased kidney is removed, the question arises if the healthy kidney can be infected by an ascending route from the bladder. That it could was formerly the prevailing opinion (145) as already stated.

Attempts to produce experimental infection by introducing tubercle bacilli into the bladder with ligation of the urethra, were made quite early, but without success (146). It was only after tubercle bacilli were injected into the ureters or into the pelvis with obstructed ureter, that the desired result was obtained (147). But recently, Wildbolz was successful, after causing a backflow of urine into the pelvis by sudden pressure on the

bladder filled with tubercle bacilli, in imitation of the above cited experiments (pyonephrosis) of Lewin and Goldschmidt (109). In human pathology, such sudden pressure increase occurs in the inflamed bladder from contraction, especially when there is the added factor of rigidity of the ureteral orifices infiltrated with inflammatory products. The experiments of Wildbolz were confirmed by Sawamura, and thus the possibility of an ascending tuberculosis cannot be doubted. Rovsing (148) as further evidence, has reported some interesting cases. Thus, it is clear that care must be exercised in the cystoscopy of such patients. It seems natural in all these experiments in which bacteria enter the pelvis after sudden pressure on the bladder, that the injury to the pelvis observed by Marcus (132) must favor the invasion of the organism.

In males, *tuberculosis of the generative organs* is in close relation to renal tuberculosis. Remarkably often (43 per cent. of the cases according to Simmonds (149)) a combination of testicular-vesical tuberculosis with vesical-renal tuberculosis is found, and Wildholz considers the higher mortality in males from tuberculous nephritis due to the frequent combination of this disease with tuberculosis of the genital organs (150). The actual cause of the combination is unknown. The opinion of Kramer (151) that congenital infection of the fetal kidney may occur, can only be applied in rare exceptions. In isolated cases, *i.e.*, those described by Rovsing, the connection is plainer, although such cases also are exceptions. Generally speaking, only isolated facts can be noted, *e.g.*, occasionally in testicular and renal tuberculosis, the bladder is not infected. Of course, this does not exclude the possibility that bacteria may reach the bladder from the testes, and then ascend to the kidney. But according to the statements made above, this is rare. The reverse route is also conceivable, *viz.*, that urine containing tubercle bacilli in flowing over the orifice of the vas deferens may have led to an infection of the seminal vesicles and testes.

The results of investigations of Baumgarten and Kramer (151) are in conflict with this conception, although they occasionally obtained a tuberculosis of the base by injecting tubercle bacilli in the bladder of a rabbit. Testicular infection was never produced, while primary testicular tuberculosis always led to an infection of the prostate. Baumgarten concludes that the nonmotile tubercle bacilli cannot move against the current of secretion, and that, therefore, tuberculosis of the epididymis is a primary hematogenous infection. But it is always dangerous to draw conclusions in relation to human pathology from negative animal experiments, and the theory of primary infection of the epididymis has by no means been generally accepted by clinicians and pathologists (149).

Baumgarten and Kramer (151) do not dispute that tuberculosis of the prostate and seminal vesicles can develop secondarily from the passing urine, or as an extension from the base of the bladder, but admit the possibility of infection from the blood. At any rate, not rarely, isolated cases of tuberculosis of the prostate and seminal vesicles are seen without involvement of the testicle. But that tuberculosis of the seminal vesicles cannot invade the epididymis is disputed by Teutschlander (152) on the basis of a large amount of autopsy material, very carefully examined. He points quite logically to the fact, that all of the secretory currents may be completely changed if the seminal vesicles are inflamed. It is naturally quite clear, that if abscesses are present, the pressure of the pus overcomes the secretory pressure, and thus leads to a spreading of the organisms towards the testes. This also would be true, if it is assumed that tuberculosis extends from the testis towards the urethra; here also, the secretory pressure would play no part, because the tubules swell on account of the inflammation and atrophy. Even if a primary tuberculosis of the testis is assumed, it is the pressure of the pus, and not the secretory pressure which determines the further extension of the bacilli.

Loeb (153) was the first to demonstrate by electrical stimulation of the hypogastric nerve, that antiperistaltic movements may occasionally occur in the vas deferens and the seminal vesicles. Oppenheim and Loew (154) repeated these experiments, and by means of electrical stimulation of the vas deferens and the injection of pyogenic organisms into the bladder, they obtained an epididymitis in their animals. In acute inflammations, in which it is generally assumed that extension occurs through the vas deferens to the epididymis, antiperistalsis may play a certain role, but in chronic inflammations, the explanation of Teutschlander appears more acceptable. In addition to this, Baumgarten (155) and Kappis found that if the vas deferens were ligated by a thread which had been saturated with bovine tubercle bacilli, the infection spread in the vas deferens towards the testis, without reaching the epididymis. Although the writers themselves drew certain deductions regarding the influence of the secretory current in the spread of the disease, the results appear more like a pretty proof of the opinion of Teutschlander.

We cannot discuss all the opinions for and against primary tuberculosis of the epididymis, but a simple clinical reflection may be mentioned. Inflammations known to be metastatic always attack the testicle first, not the epididymis (see orchitis in mumps). Kramer believes that infection of the epididymis is a peculiarity of chronic infections, since it also occurs in leprosy. This reasoning is not convincing, especially since we find tubercles in the testes, in the metastatic distribution of miliary

tuberculosis, and since Janis and Nakarais (156) found tubercles in the healthy testes of phthisical patients.

Tubercle bacilli travel interstitially from the epididymis, or by way of the lymph channels to the testis (Simmonds). According to Ash (150) experimental injection of tubercle bacilli or tuberculin into the internal spermatic artery causes a fibrous inflammation of this organ, with proliferation of the cells of the spermatic tubules. Whether the periods of erotic excitement in so many consumptives are actually related to this, as Asch thinks, does not at present seem proven by these experiments.

Previous trauma favors the development of testicular tuberculosis. Thus Simmonds observed the condition in a rabbit after contusion of the testis and intravenous injection of tubercle bacilli. It is also very remarkable that it practically always develops during the reproductive period. It is not very certain how this is to be explained. Dette Santi (157) thinks that engorgement with blood is of importance. He obtained a tuberculous orchitis in guinea pigs by the injection of tubercle bacilli into the urethra after having ligated the spermatic vein, but in this experiment, "trauma" to the testis is unavoidable, and it proves little in relation to the influence of hyperemia.

The whole question of the pathogenesis is of great interest for therapeutic reasons. If it is a primary disease of the testis, its removal promises much better results than if the seminal vesicles and prostate are involved. Conversely, attempts to decide whether the testicle alone was diseased have been made from the results of castration. All the conclusions, however, appear to be problematical, because it is only in certain isolated cases that we suppose, merely with a certain probability, that there is tuberculosis of the seminal vesicles; accurate diagnosis is impossible.

*Renal and vesical calculi* are diseases which have a certain geographical distribution (158). Renal calculi are rare in Germany, only in Württemberg and Altbürg they are, or were, more frequent (159). The reason for this regional difference is, of course, not known with certainty. But since their formation is rare in countries of high culture, the supposition is that primitive hygienic conditions, especially an unbalanced diet during childhood, are the cause of their formation (Schlagintweit, Kuttner). In Egypt (160) where vesical calculi are often found even in children, the frequent entrance of parasites through the urethra into the bladder (bilharzia), is supposedly the cause of their formation (161).

[The impressive statistical fact has been reported by Osborne, Mendel and Ferry that of all rats fed on experimental rations deficient in fat soluble vitamin there was formation of phosphatic calculi in every case (162).]



It has already been mentioned in discussing gall stones, that their formation in the human body is a problem in colloid chemistry (163). This applies as well to urinary calculi. The urine cannot be considered simply as a salt solution (crystalloids), it contains various colloids also. According to Schade, "the relations of both may be pictured as a salt solution suspended in the spaces of a more or less connected scaffold, consisting of a very diluted jelly." It holds more salts than a corresponding amount of water could dissolve; and it is due to the colloids present, that the salts are not precipitated. Even larger quantities of crystalloids may be suspended in such a solution; and the conception which held sway for some time (164) that their formation depends on an increased formation and excretion of uric acid—the uric acid diatheses or other salt—and that it is in close relationship to gout, cannot now be accepted (165). Ebstein (166) had already called attention to the fact that there are diseases with markedly increased uric acid excretion without calculus formation, *e.g.*, leukemia. But precipitation of these crystalloids and colloids takes place when "the stability of this system" is disturbed (Lichtwitz). A deposit of mucus and crystals is, of course, frequently seen when urine is allowed to stand, but such a mixed deposit of crystalloids and colloids never forms a calculus even if it is permitted to dry out, but remains a friable grumous mass which can easily be redissolved. It differs from a urinary calculus in that the latter is laminated, *i.e.*, layers of colloids and crystalloids alternate; furthermore, the colloid will not dissolve, *i.e.*, it is "irreversible."

Schade, by using an irreversible colloid-fibrin—succeeded in producing experimental, laminated calculi, which showed great similarity to urinary calculi. Since fibrin is added to the urine in inflammations, this latter process must be considered a factor favoring calculus formation; and Studensky (167) actually obtained calculi after introducing a foreign body into the bladder of the animal, but only after a catarrh of the mucosa developed. If inflammation did not occur, no deposit whatever was formed on the foreign body. A foreign body *per se*, therefore, favors calculus formation not by becoming a nucleus of crystallization, but only insofar as it causes inflammation. The fact that the calculi are found massed around the foreign body can be explained by the relatively great surface tension at the contact points of foreign body and urine (Schade).

It must not be assumed from the foregoing experiments that there is a demonstrable and regular connection between the formation of urinary calculi and inflammations of the urinary tract, since we find far more urinary tract inflammations without calculi than with them. It is not every kind of inflammatory process which leads to this characteristic precipitation of colloids and crystalloids.

Fibrinuria may be present without any inflammation in the urinary tract, *e.g.*, with suppurating processes elsewhere in the body (168). But the colloid involved in the precipitation does not necessarily need to be fibrin, for other colloids have this same property (Schmidt). Ebstein and Nicolaier (169) consistently obtained renal calculi in animals by feeding oxamid for several weeks, and Tuffier and Rosenbach (170) *a.o.*, repeated and amplified these experiments with similar success. Since oxamid feeding leads to an injury of the renal epithelium, the above mentioned essentials for the formation of calculi are obtained. Their presence in osteomalacia and other bone destroying processes is perhaps a certain, although loose analogy, and we may assume in these diseases that the salts derived from bone destruction favor their formation in a manner similar to that in oxyamid feeding (171).

Therefore, we speak nowadays of a precipitation of irreversible colloids and crystalloids in the formation of urinary calculi. But this is only an amplification of the fact discovered by Ebstein, that each calculus consists of an organic scaffolding which encloses crystalline salts, and that all these calculi grow by further deposits of salts and organic substances. This finding has often been verified (172). Chemical analysis has shown that the crystalloids consist for the most part of calcium oxalate and uric acid, although pure uric acid calculi are rare (173).

How they act as foreign bodies, and cause all kinds of injury to the kidney, especially to the pelvis, has been studied experimentally by Kumita (174). His experiments are not very enlightening, since the damage from operative trauma, urine retention, infection, etc. cannot be differentiated, although they do imitate the findings in calculous nephritis. There are the combined influences of the presence of foreign bodies, retention of urine, and infection, all of which necessitate operative interference, not for the calculus itself, but for relief of its sequelæ.

It might be mentioned that calculi are occasionally crushed spontaneously in the bladder by its contraction (175).

The *nerve supply of the urinary bladder* has again awakened considerable interest both on account of the numerous gun-shot wounds of the spinal cord with paralysis of the bladder, and because of the increase in the most diversified functional bladder disturbances, especially enuresis, appearing during the war.

It is very similar to that of other internal organs (176). Numerous ganglion cells which exhibit a pronounced independence are present in its walls. Zeissl showed that the bladder will continue contracting periodically when all afferent nerves have been cut, and O. B. Meyer (*cit.* by Muller (133)) observed an animal's bladder which was removed, empty itself by contraction after it was filled through the ureter. This indepen-

dent function is regulated by afferent nerve fibres, however, and as in other internal organs, the innervation is double, their functions being opposed. They are first, the sympathetic hypogastric plexus coming from the lumbar cord, and secondly, the sacral autonomic pelvic nerve, or erigens, from the sacral end of the cord. Both nerve groups not only supply the musculature of the bladder but also the internal sphincter; while the external sphincter receives separate twigs from the pudendal nerve. Ganglion cells are located in the hypogastric, and in the pelvic plexuses, and altogether, the more minute ramification of these nerves is very complex.

Stimulation of the hypogastric plexus causes closure of the internal sphincter and relaxation of the bladder (detrusor muscle), and conversely, stimulation of the pelvic nerve or erigens causes dilatation of the internal sphincter and contraction of the bladder. This peculiar condition, when stimulation of a nerve causes contraction of one muscle, and relaxation of another is called "crossed innervation" (Busch). The nature of this is not very certain.

The hypogastric nerve is controlled from the lumbar cord, and the pelvic nerve from the sacral cord (177). Thus, as Muller now emphasizes emphatically, there are two separate centers for the bladder which are united partly directly, partly indirectly, through reflex relations with all the sensory tracts of the body surface. This explains the urgency of urination in patients, especially children, from painful sensations such as operations, dressings, etc. Furthermore, there must be relations between the brain and the bladder centers, although their course is at present as little known as the location of the bladder centers in the brain itself. Kleist and Forster (*cit.* by Muller) have indeed reported the interesting observation that in bullet wounds of the brain, difficulty in urination is present in those cases in which there is a bilateral paralysis of the feet present at the same time. This suggests that a bladder centrum exists in the temporal apex, and only bilateral destruction will produce symptoms. Disturbances of bladder function have also been described in focal softening in the large root ganglia (178); and in animal experiments, bladder contractions have been elicited by stimulation of this area (179). In short, a number of facts are known which indicate that we may expect bladder disturbances in cerebral disorders, especially injuries, but thus far, very little interest has been shown in this question from the surgical viewpoint.

Apart from the disturbances in the motor tracts, there are also disturbances in the sensory tracts which lead to changes in bladder emptying. That the urethra is very sensitive to pain can be quickly shown by catheterization; it is also sensitive to temperature differences. The sensitivity

extends throughout the urethra, but it is not known whether it is present everywhere to the same degree, both qualitatively and quantitatively. In regard to the sensitivity of the bladder itself, the opinions of writers differ considerably. R. Zimmermann, prompted by Muller (180), made experiments on himself, and found that the touch of a metal catheter was only perceived at the vesical sphincter, and that the bladder was unable to distinguish between ice water and water at 45°C. Other authors such as Frankl-Hochwart-Zuckerkindl, assert that the bladder is very sensitive to temperature differences and also to electrical stimuli. Muller believes that sensation is elicited only by contraction of the musculature. My own observations during cystoscopies, have shown that many patients with a normal bladder do not feel the touch of the ureteral catheter at all, while others react immediately. Systematic investigations are necessary to clear up this question. In numerous operative cases, in which the high frequency current was used for its heat effect alone, pain was felt only if isolated areas were exposed for some time. This would support the opinion of Muller. But these findings cannot be considered decisive. Muller was able to elicit neither touch nor temperature sensation in vesical exstrophy. With this uncertainty in regard to the simplest facts of vesical sensitivity, it is natural, that we have even less information concerning the factors causing spontaneous sensations in the bladder. We know that filling causes no sensation whatever at first, and only after it has reached a certain degree, is the impulse to urinate perceived; severe pain is felt later. Even in this, it is absolutely unknown whether the pain is a result of bladder distention, or due to attempted muscle contractions (Muller).

It is also uncertain how the desire to urinate is brought about. Posner, Finger (181), a.o., are of the opinion that when the bladder has reached a certain degree of fullness, urine is forced into the prostatic part of the urethra, and this distention of the posterior urethra, which is, of course, still closed by the external sphincter muscle, causes the desire to urinate. Other authors believe that the distention of the bladder itself is felt and this incites the desire to void; others think that sensation is roused by the contraction of the vesical musculature. None of these theories can be seriously entertained, until our knowledge of vesical sensitivity in general is more definite. Naturally, it is indisputable that certain sensations which influence the voiding of urine arise within the bladder.

Frohlich and H. H. Meyer (182) have studied the route by which these sensations are carried to the spinal cord and to the brain; and according to them, they are transmitted by the pelvic nerves, because after cutting through the posterior roots of the sacral cord, the bladder becomes insensitive to the faradic current. The sphincter area contains sensory fibres



from the pudendal nerve. Finally, according to their experiments, the hypogastric plexus has nothing to do with sensitivity.

It is obvious that most diversified vesical disturbances can be caused by changes in this complex nerve supply, but thus far, these have been only partly analyzed.

The internal sphincter usually maintains a certain tension—tonus—which, as is well known, persists in the cadaver (Rehfish) and, for this reason the bladder is usually found filled at autopsy. This intermediate tonus is also quite sufficient to retain the bladder contents in the living. Stimuli for the opening of the sphincter internus are, as already stated, carried by way of the pelvic nerve or erigens. If the stimulus is absent, or the internal sphincter fails to react, retention of urine is the consequence. From the preceding, it is easily seen that no abnormal resistance to the introduction of the catheter need exist in these cases. This form of retention is not very rare in children (183). By anesthetizing the pudic nerve separately from the sympathetic and the sacroautonomous fibres, which are only met with in the prostatic region, it can be decided in such cases whether the innervation of the internal or of the external sphincter has been disturbed (Rost). This form of retention corresponds to that obtained by bilateral section of the pelvic nerves; cutting of the hypogastric nerves does not cause any noteworthy disturbance (Muller).

According to Zollner, a similar difficulty in voiding is also found in sensory disturbances within the area of distribution of the pudic nerve. But thus far, these findings, which are of general interest in the physiology of urination, have not been verified by other authors. It should not be difficult to confirm this observation by anesthetizing the pudic nerve.

It is, therefore, possible to examine sphincter function to a certain degree by the use of separate anesthesia of the pudic nerve and of nerves surrounding the prostate. The power of the detrusor can be estimated by means of manometric investigations of the urine pressure, but unfortunately the abdominal pressure cannot be quite eliminated in these tests, and this plays considerable role in restless patients (184). The hyper-tonicity of the detrusor can also be diagnosed with some degree of certainty from the presence of a trabeculated bladder, which, therefore, is not merely a sign of difficult urination.

Schwarz has investigated a large number of cases of spinal cord injury by these methods and found all conceivable combinations of detrusor conditions on the one side, and sphincter conditions on the other. The level of the injury had no recognizable influence on the type. In the majority of cases it was found, clinically, that "automatism of the bladder," as it has been called, was present, *i.e.*, the bladder emptied itself periodically, without the intention or knowledge of the patient. There

had often been a previous total urinary retention. It is known that the bladders of patients with spinal cord injuries usually contain residual urine, a symptom which is characteristic also of other diseases, *e.g.*, prostatic hypertrophy. Its cause is unknown, but according to Schwarz, there are two possibilities; either the bladder does not feel small quantities of urine as a stimulus to urination, the detrusor then contracts only as far as its threshold; or some anatomical changes prevent complete evacuation. Thus far no certain differentiation can be made.

The *absorptive power* of the bladder and urethra was investigated by Treskin, Maas and Pinmer (185), apart from the older works of Segalas, Orfila, Demarquai, Brown-Sequard. According to these studies in which different substances such as iodine, pilocarpine, strychnine were used, it has been proved that certain of them are absorbed by the bladder and introduced into the circulation, but according to Treskin, no absorption of water takes place. It is especially important for modern surgery to know that local anesthetics, such as cocaine and eucaine, are absorbed, and may lead to severe toxic symptoms if they are permitted to remain in the bladder after an endo-vesical operation. Urethral absorption is perhaps even more active, as various observations regarding cocaine poisoning have shown, but it must not be overlooked that the anesthetic is greatly diluted in the bladder, which is not the case in the urethra. These deductions are therefore permitted with the described reservations.

The normal bladder is free from bacteria, but with the onset of inflammatory changes bacteria are present in the majority of cases, the usual organisms being the colon bacillus; staphylococci are rarer (186). Exceptions to this rule occur on both sides. Thus E. Becker, and Strauss (187) have recently described cysto-pyelitis observed during the war, with urine rich in leucocytes, but sterile. On the other hand, bacteriuria is found without inflammatory changes in the bladder. As already mentioned in discussing pyelitis, a change in the bladder and pelvic mucosa can be obtained in animal experiments only when retention is produced at the same time, or if the bladder mucosa is traumatized, as in the work of Bumm (188).

The mucosa of the bladder and of the pelvis which is normally free from bacteria, possesses, therefore, a protection to infection, and injuries, usually traumatic, must be added in order that catarrh develop. Gynecologists frequently observe post-operative cystitis if the bladder has been stripped for some distance from its adjacent organs (188), and the cystitis appearing after childbirth may also be considered secondary to traumatic injury of the bladder walls. But cystitis due to retention is more difficult to understand. It is, of course, assumed that the bladder mucosa is irritated by the decomposition products of urine, such as the ammonia formed

from urea (189). Rovsing actually differentiates between bacteria which split urea, and those which do not. According to Leube the urea of normal urine cannot be decomposed except by bacteria, and Musculus, accepted this statement for some time. But possibly the vesical mucosa may be irritated by various other chemical substances.

*Pollakisuria*, or increased desire to urinate, so generally observed during the war, is probably the slightest form of such irritation. Its cause is by no means clear. If pollakisuria is combined with polyuria, then increased salt content of the food and increased intake of fluids must be held responsible for the latter, but perhaps the food also contains other diuretically acting substances (Strauss). In some cases of pollakisuria, ammoniacal fermentation is assumed to occur (190), or it is explained by an old cystitis, psychical factors, colds, etc. (Strauss). But all these things can be only occasional factors. Why could not some chemical substance, derived from the food, and excreted in the urine, cause vesical irritation? It does not absolutely refute the possibility of the presence of such a chemical stimulant, that pollakisuria causes no anatomical changes in the bladder; the wide spread prevalence rather supports it. The vesical catarrh caused by drinking recently brewed beer must be similarly explained, but we know very little of the nature and chemical composition of such irritating substances. Comparatively speaking, we are best informed of those irritations of the bladder mucosa due to the chemical substances used in the anilin industry (191). There is no basic difference simply because in these cases, it may finally lead to carcinoma, or that the cystitis itself may almost disappear. The fact remains that workers in anilin plants are subjected to a chronic irritation of the bladder mucosa, due to the excretion of a chemical substance, (Leueberger supposes this to be a hydroylated aromatic amide compound). It is often evidenced only after years; carcinoma frequently appears when the workers have not handled the dangerous substance for a long time (Oppenheimer).

We know even less of other injuries to the bladder mucosa than we know of the urine soluble chemical substances which irritate it. "Cold," of course, plays a large part and especially a local cold acting on the vesical regions. It is known that women acquire cystitis after very cold douches; and patients with prostatitis suffer frequently from retention after sitting on a cold stone, for example. But it is entirely unknown whether in these two cases a cystitis is at fault, or a functional disturbance of the sphincter (Rochet).

Injuries to the urinary bladder, apart from those due to bullets and stab wounds, are, in the great majority of cases, caused by an abdominal blow striking the filled organ. *The physical and physiological aspects*



of rupture have been studied by numerous workers. Houel, Dittel, Ullmann and v. Stubenrauch first investigated the pressure required to rupture the viscus by filling with fluid (192). v. Stubenrauch found that "the average weight required to just tear a strip of bladder wall 1 cm. broad, without considering its thickness, approximated 1.5 kg." If the pressure which just ruptured the bladder was estimated by filling it with water the figures were somewhat less constant. On the average, it amounted to 0.5 kg. with a minimum of 0.15 kg.; in the same way, the quantity of fluid required to fill the bladder sufficiently to cause rupture, also varied (from 300 to 5000 c.c.). These figures show that in practice, it is hardly possible to say how far the bladder may be filled without danger. Stubenrauch also investigated the elasticity of the bladder in relation to traumatic rupture, but he himself is of the opinion that the data obtained in the cadaver proves nothing for the living. Berndt imitated natural conditions more closely; instead of causing rupture by filling the bladder through the urethra, as in the experiments described, he filled the bladder to a certain degree and then delivered a blow against the abdominal wall of the cadaver. As he correctly emphasized, the important practical question is, why does the bladder rupture not only on its posterior and upper part where it lies free and is struck, but also quite frequently through its anterior and lower walls even if the blow strikes the bladder from above? As a result of these experiments, Berndt concludes that the internal pressure of the bladder is increased by a blow against it, and that the bladder tears where its surroundings offer the least resistance. With a very full bladder, the upper and posterior parts are torn; when it is partly filled, those parts are torn close to the yielding tissues in the pelvic floor. Pressure against the promontory and other bones in the vicinity is probably not as important as was thought (Bartels). The direction of the tear is usually longitudinal, which Berndt, as well as v. Stubenrauch considers due to the arrangement of the musculature, but Bartels states that the direction of the tear varies. It is usually from within outward, and, therefore, incomplete tears are often found, *i.e.*, tears of the mucosa only, which naturally have a more favorable prognosis.

It is also important in the treatment to discover whether the peritoneum is torn or not. In the first instance the urine pours into the abdominal cavity and the bladder is empty. A remarkable symptom in these patients is the strong desire to micturate and it has been mentioned above that we do not know any details of the cause of this desire. At any rate, in such cases an inflow of urine into the prostatic urethra is probably not responsible (Posner), but we do not know how soon after injury this urgency appears, or if it depends on the position of the tear. In injuries involving the peritoneum there is considerable absorption of urine, as



investigations of Oehlecker and Rost (193) have shown. In animal experiments, Rost found by the retention of nitrogen in the blood, that the animals died of uremia after intraperitoneal vesical rupture, before peritonitis developed. This fact is of practical value, inasmuch as it seems unwise to delay operation in this condition until peritonitis develops. The results of these animal experiments hold good in man. Peritonitis develops only if the urine contains organisms or is infected by later catheterization. Uremia from absorption of urine is the condition to be feared in these cases, as shown in the patients of Oehlecker, by an increase in the freezing point of blood.

*Wounds of the bladder heal very quickly, and the regenerative power of the urethra* is also exceptionally great. Virgli (194) who systematically investigated experimental vesical wounds could scarcely find the scars after a few months, and it is on account of this exceptional ability to heal, that other tissues such as omentum or bowel can be used so successfully in closing openings in the bladder (195). In dogs, Rost repeatedly saw rapid healing of cuts large enough to establish wide communication between the bladder and the abdominal cavity, without having attempted to provide a closure operatively. That the urethra also quickly and completely regenerates, is well shown in the healing of the defects, several centimeters in length, produced by prostatectomy. Ingianni (196) found that not only epithelium, but the corpora cavernosa can close this gap in a short time by budding, but the musculature does not regenerate. The new formed epithelium consists first of one layer and later of several.

The *function of the sphincters* must be discussed in some detail. The external sphincter consists of striated muscle fibers; *i.e.*, it is under the control of the will, and is innervated by the pudic nerve. After the work of Rehfisch (197), it is now the general opinion that it only serves to retain up until the last instant the urine which has passed into the prostatic urethra. It is supposedly not involved in the actual emptying of the bladder. Rehfisch assigns a special importance to the internal sphincter, which is placed annularly around the bladder orifice. As stated above, he recognized that this sphincter is kept closed by an inherent tonus, and opens voluntarily only during the act of micturition. Naturally, it is of the utmost practical importance to know in operations near the sphincter, *e.g.*, prostatectomies, whether or not the control of the bladder depends more or less entirely on this one muscle bundle, the internal sphincter. Now Lendorf (357) showed by examinations with Goldschmidt's urethroscope, that not only the internal sphincter, but the whole of the prostatic urethra participates in the closure of the bladder. Indeed, the closing power of the internal sphincter is weak and its resistance is more easily overcome by the catheter, than that of the external sphincter. Lendorf

repeatedly observed an open internal sphincter in patients perfectly continent after prostatectomy (198), and he explains the observation of Freyer (Allen) that after prostatectomy ejaculation occurs not outside, but into the bladder, by this open position of the sphincter. In great urgency (Lendorf), or in those symptom complexes such as prostatism or functional retention of urine in children (183), in which there is overfilling of the bladder, it is found that the internal orifice is not firmly closed and ring-like, but the bladder continues funnel shaped into the prostatic urethra. It is easily understood that an infection of the bladder is favored by such conditions.

As Lendorf could see with the urethroscope, the internal orifice assumes a triangular shape with the apex anteriorly when the sphincter opens. He deduces from this that the internal sphincter not only opens actively, but that there is a simultaneous pull by the detrusor fibres which enlarges the opening.

The disease which is probably the most frequent cause of disturbances in the activity of the sphincter, particularly in producing greater difficulty in micturition, is *hypertrophy of the prostate* (199). In spite of the many theories which have been advanced to explain its cause, the subject still has its original difficulties. It may be stated, however, on the basis of careful pathological anatomical investigations that the inflammatory processes found in hypertrophied prostatic glands are probably secondary (Runge, in contradistinction to Rothschild (200)). According to Loeschke, the hypertrophy does not develop, as assumed by Marion and Lendorf (201) from the periurethral glands, but it begins in the muscular portion and forces the muscle bundles apart. Loeschke narrows down the old opinion of Guyon, that it is a result of general arteriosclerosis, by showing that only those branches of the prostatic artery which belong to the portion undergoing hypertrophy, show arteriosclerotic changes.

We are somewhat better informed of the mechanism of difficult micturition in this disease. Of course, it is quite natural to assume that enlargement of the organ diminishes the lumen of the urethra, somewhat like a stricture. But this idea is incorrect, as shown by the fact that even a thick catheter will pass easily if it has the right curve, and the difficulties in catheterization are, therefore, not avoided by the use of a thin catheter. The different theories which relate the retention of urine in this disease to all sorts of mechanical peculiarities of the vesical orifice or the urethra, such as valve formations, etc., only hold in single cases. The plaster casts of the bladder and urethra made by Reerink (202) have shown with certainty that the prostatic urethra is not narrowed, but enlarged [in hypertrophy of the prostate, and therefore, the obstruction to urination is evidently not at the exit of the bladder. The opinion of Lendorf, generally

speaking, seems well taken, *viz.*, that the function of the internal sphincter in producing micturition by active opening, is impaired because a swelling develops between the muscular layer and the urethral mucosa, separating the musculature from the mucosal tube. Then the sphincter of the bladder acts only as a closing muscle—not as dilator. But the difficulties in micturition do not always begin as slight difficulties which gradually increase to complete retention, but retention may develop with astonishing rapidity and may continue for years or permanently, after a single catheterization. We do not know what causes this complete retention. A failure of detrusor action caused, for example, by overfilling of the bladder from an unusual intake of fluids (203) is usually assumed. Conversely, other authors consider the sphincter the cause of the acute disturbances (204), and speak of an inflammation or swelling of the gland which prevents the sphincter from carrying out its task, *i.e.*, the opening of the vesical orifice.

As has been mentioned above, hypertrophy of the prostate does not lead to a uniform enlargement, but to an adenomatous tumor-like formation within it, and especially in its muscular part (Loschke). In prostatectomy, we shell out these tumor nodules, and the closing power of the bladder can be, and is, repaired by means of the remaining prostate and muscular layers. So-called continence develops, however, in the majority of cases, even after complete removal of the prostate, *e.g.*, in carcinoma. Whether in such cases certain muscle bundles of the bladder assume the function of a sphincter is not known (see also p. 321).

Resection of the vas deferens or castration was formerly much in use, in the treatment of hypertrophy of the prostate, although it is rarely employed at present (205). These so-called “sexual operations” were based on a not very well understood relation between prostate and testes.

In regard to the physiology of the gland, we know, in addition to the above discussed function of vesical sphincter, that it adds a watery secretion to the seminal fluid which activates the motility of the spermatozoa (206). Notwithstanding the work devoted to studying a supposed internal secretion, nothing has been proved (207), although we know from autopsies of eunuchs, human and animal, that early removal of the testes in adults as well, leads to atrophy of the prostate and seminal vesicles (lit. see 207). But whether this is caused by the absence of the external testicular secretion and function, or by the absence of an internal secretion of the same organs, is not known. Deductions have frequently been carried very far, and in particular, the improvements in the disturbances of prostate patients after operative treatment, have been compared to the atrophic processes in the normal gland. But this does not seem correct, because hypertrophy of the prostate is a new growth and cannot simply be regarded

as an enlargement. The fact remains that in no case that could be investigated by autopsy, was shrinking of an hypertrophic prostate demonstrated after castration or vasectomy (Schlange). Probably the relief of patients operated by these methods is due only to a subsidence of a swollen prostate and not to a shrinking of the actual tumor. A fresh specimen will show that these hypertrophic prostates are remarkably "adenoma like."

These considerations apply equally as well to animal experiments in which attempts are made to bring about reduction in the size of enlarged prostates by x-ray treatment of the testes. The illogical deductions result from the mistaken analogy between the prostate and the uterus; and hypertrophy of the prostate and uterine myomata (208). Embryologically the prostate is entirely different from the uterus. And after the negative results of treatment, enlargement of the prostate cannot be compared to uterine myomata. Of course, all these considerations are not intended to discuss the value of the sexual operations, but are only directed against mistaken pathological conceptions and the conclusions derived from them.

In connection with the influence of *castration* on the prostate, a few words must be added in regard to the general results of this procedure (207). According to the statements in the literature, removal of both testes on account of tuberculosis, causes very few symptoms from abolition of function, psychical disturbances in particular are very rare (209). The reason for the inconspicuous symptoms is due not alone to the fact that the individuals castrated for tuberculosis are mostly adults, but the sequelae are masked by other disease symptoms. Perhaps, however, special investigations would discover some symptoms due to the loss. On the other hand, in castration for injuries, all kinds of symptoms, especially psychic disturbances, develop. Lichtenstein (210) reports a very carefully observed case in which melancholia and depression, disturbed sleep, cries during sleep, etc., were present, and Bauer (84, p. 97) describes certain peculiarities in a man castrated at the age of 25. There is no doubt that the temperament changes after operation; the patient becomes more sedate and phlegmatic; a fact utilized since olden times for pastoral purposes especially in horse and cattle raising. Sexual impulses arising in the brain are supposedly undisturbed by castration; but according to Tandler and Gross (211) all statements made by castrated individuals with regard to impotence must be accepted with great caution. At any rate, observation shows (Lichtenstein) that all sexual functions are completely suspended after castration.

It is, of course, of the greatest practical interest to know whether these symptoms due to the loss of organic function are consequences only of the loss of internal, or also of the loss of external testicular secretion.



This question has been studied very often. Hunter demonstrated that roosters lose their male characteristics after castration (capons), but retain them if the testes are implanted elsewhere in the body. These experiments he repeated in various forms with similar results (cit. by Lichtenstein). Steinach (212) carried out such experiments on a large scale with rats and showed that disturbances due to castration, *e.g.*, atrophy of genitalia, will not occur if the testes are implanted in the abdominal musculature. From his experiments, it may be accepted that many specific sexual properties are the results of the activity of the internal secretion of the reproductive glands and that at least in animal experiments, it is possible to produce changes. Lichtenberg who drew practical deductions for human pathology from them, implanted an undescended testis removed from another man, directly into the abdominal musculature of a patient, who had suffered considerably from psychical and genito-functional symptoms, due to the loss of both testes (trauma), with the result that the psychical disturbances disappeared and sexual power returned. If, as Rohleder (213) advises, this transplantation has other uses, *e.g.*, treatment of the homosexual to reestablish heterosexual desires, cannot be decided at present.

The disturbances are especially pronounced in individuals who are castrated in youth; a custom in vogue among some people and religions (Tandler and Gross (211)). Physically, the abnormal obesity is noteworthy, and points to changes in metabolism. Examination has shown these changes are due to decrease in oxidative processes, but we are little informed of other details, especially of the metabolism of salts. The excessive obesity affects certain portions of the body, especially the hips, the breasts, etc. and domestic animals are castrated that they may be fattened. Bone growth is increased, but it is not clear whether it is a direct result of castration, or indirect, through the influence of the thymus, since the involution of that structure is, as will be discussed later, closely connected with the development of the testes. But notwithstanding its size, the body of the eunuch remains in an infantile stage, especially the larynx. The voice remains high pitched. The growth of hair on the body is absent, while that on the head is abundant.

As already stated, these symptoms just described are rarely seen, after operative castration, because this is usually done on adults. But constitutional changes of the type described, are known, and justify the assumption of a hypoactivity of the testicle. Of course, as in most diseases of the ductless glands, in such cases it is not merely the absence of the testes, but involvement of other endocrine glands, especially the hypophysis cerebri, which adds to the complexity of the disease picture. The hypophysis in such cases is said to supply insufficient secretion (hypo-

function). According to Bauer (84 p. 95), in so-called "eunuchoidism," two very different types must be differentiated—the eunuchoid tall type, with graceful physique and long limbs must be distinguished from the eunuchoid obesity. Often the wrinkled condition of the face is very pronounced, giving the patients a senile appearance (geroderma).

The reverse, *i.e.*, a sexual precocity, has repeatedly been described in children with testicular or ovarian tumors, *e.g.*, carcinoma of the testicle (Sacchi, cited by Bauer). Thus, in a nine year old boy, a beard, masculine voice, hair on the trunk, libido, etc. developed, and all these symptoms disappeared after removal of the tumor. In other cases, this precocity is not connected with the sex glands, but is possibly related to changes in other endocrine organs, especially the *pineal gland*. We deduce a retarding influence of the pineal gland on sex development, from the fact that its destruction by tumors in boys causes sexual precocity and marked growth in height, growth of hair, etc. (214). These clinical observations correspond with experimental results (see Biedl (384)). The pineal gland has thus far not been of surgical interest. Since it is a question only of hypo-activity of the organ in all the diseases thus far recognized, operation could only deal with removal of brain pressure symptoms; we can do nothing surgically for its functional failure.

It is quite otherwise with the second endocrine gland situated within the skull, *viz.*, the **hypophysis** (207). Surgery is the chief method which has increased our physiological knowledge of this organ within the last few years (215). The hypophysis cerebri is divided both histologically and physiologically into three completely separated parts, the anterior, the central, or pars intermedia, and the posterior lobes. In the organ extracts offered commercially under the names of hypophysin, pituglandol, pituitrin, etc., the material consists of a part of the central lobe and the posterior lobe. They act essentially by increasing blood pressure and by stimulating unstriped muscle tissue such as that of the uterus and intestines to contract. For this reason they are used in obstetrics. They are also diuretics. As further examinations have shown, the action depends only on the central lobe, and extracts from the posterior lobe are inactive. Nothing is known at present of the function of the latter which consists of nerve elements, but it does not appear to be in any relation to the known diseases of the hypophysis. The central lobe supplies the secretion, the action of which has been described. Colloid droplets can be demonstrated in the central duct, and they pass through the posterior lobe during excretion. It is assumed that the secretion enters the cerebrospinal fluid, but it is not known that this fluid shows an increased activity from the presence of hypophysis extract.

Extracts from the anterior lobe, apart from a brief lowering of blood

pressure, probably not specific, have no recognized experimental action. But as shown in extirpation experiments, and by observations on patients, the anterior lobe is of great importance in the growth of young individuals, and in metabolism in general, for complete removal of this organ in young animals, leads to hypophyseal cachexia and early death. Its extirpation checks growth, and the epiphyseal lines are retained disproportionately long.

It is now generally assumed that the excessive growth in length after castration does not depend on the testes, but on hyperfunction of the anterior lobe of the hypophysis. In pregnancy also, certain histological changes are found in this gland. Such excessive growth in the long axis of the limbs with underdevelopment of the sexual glands, and secondary hypersecretion of the anterior lobe of the hypophysis lead to giantism. Since the hypophyseal changes are secondary, the treatment of diseased reproductive glands need not include treatment of the hypophysis (see Biedl).

Most interesting to the surgeon are the diseases of the hypophysis which are related to disturbance of growth. In *acromegaly*, that extraordinarily characteristic disease in which only the ends of the limbs, *i.e.*, hands and feet, nose and chin, develop enormously, an adenoma of the anterior lobe of the hypophysis is found in the great majority of the cases. Thus far, the long continued controversy, whether there is an increased, decreased, or altered secretion, is by no means cleared up, but is now laid aside on account of the success of operative procedures. Since Hochenegg, we know that acromegaly can be cured by the extirpation of the hypophyseal adenoma, therefore, a "too much" is surely present, but whether it accomplishes its pathological action directly or indirectly, we do not know. In the same way it is quite uncertain how far the edematous condition of the subcutaneous tissue in acromegaly is related to a disturbance in the thyroid gland. Just as in the other diseases of the hypophysis, there are also changes in the reproductive glands in acromegaly (207). The menopause is one of the early symptoms of the disease in women. But on account of therapeutic results, changes in the sexual sphere in acromegaly must be considered as secondary.

Another disease complex related to the hypophysis is that form of obesity, known as *adipose genital dystrophy* (216). In this disease, we have an abnormal fat development in certain parts of the body with uniform underdevelopment of the genitalia. Usually, a tumor of the hypophysis is found, but not an adenoma which increases the functional activity of the hypophysis, as in acromegaly, but cysts, carcinoma, sarcoma, etc., *i.e.*, tumors which destroy the hypophysis. For this reason, it is now generally assumed that the obesity is caused by hypoactivity of

the hypophysis, an assumption which corresponds perfectly to the findings in animal experiments. A case reported by Madelung (217) offers a beautiful proof for the correctness of this opinion; obesity developed after a bullet wound in the brain, and the x-ray picture showed that the bullet occupied the exact situation of the hypophysis. Operative treatment of adipose genital dystrophy gives good results, but they are not progressive (215), (218). After some improvement, the condition remains about the same, from which Biedl concludes, that opening a cyst, or the removal of a tumor removes pressure, which permits of better secretion. This is not to be considered as proof that this form of obesity is due to hyperfunction, but on the contrary, to hypofunction of the hypophysis, especially of the central lobe. For this reason, after relieving the pressure, treatment which hypophysis extracts gives very good results.

It has already been mentioned that the hypophysis extracts prepared chiefly from the middle lobe, act as diuretics. It is, therefore, logical to assume that diseases characterized by polyuria, *e.g.*, diabetes insipidus, are related to changes, *i.e.*, hyperfunction of the median lobe. Frank (219) observed a case of diabetes insipidus which developed after a bullet wound in the head and in which the missile was situated close to the hypophysis. He assumes that the bullet acting as a constant irritant to the gland, caused hypersecretion. Simmonds (220) describes a case in which the metastasis of a carcinoma involved the sella turcica. The polyuria which was present, he supposed to be due to irritation of the pars intermedia. Conversely, other authors consider diabetes insipidus due rather to a hypoactivity of the hypophysis (see 84), because treatment with pituitrin has repeatedly given good results. All these questions, including the relations of the pituitary gland to dwarfism, especially to chondrodystrophy (Biedl) are still unanswerable. We require much more precise information in all directions.

The *internal secretion of the testes* discussed above is due to the interstitial cells, according to our present opinion. Very instructive in this relation are the experiments of Tandler (221) who exposed the testes of fallow deer to x-rays, obtaining, thereby, complete destruction of the sperm cells while the interstitial cells remained intact. In the animals so treated, the antlers grew normally after having been shed; although castrated fallow deer as controls, grew a misshapen pair of antlers, the so-called perugue antlers.

The sperm cells are far more sensitive to injury than the interstitial cells. This applies especially to nutritional disturbances and the testicular blood supply with the results of its interruption have been the frequent object of experimental investigations (222). It was found that after ligation of the internal spermatic artery, a hemorrhagic infarct of the



testis develops very quickly, while the epididymis, which is supplied by the deferential artery, is less injured. According to investigations of Enderlen, the testicle tolerates the ligation of the spermatic cord, *i.e.*, all the vessels, including the veins, for about 16 hours, without showing microscopical lesions. This is important in the prognosis of torsion of the testicle. The organ recovers even after longer ligation, but spermatogenesis suffers, and subsequently a gradually increasing atrophy of the organ takes place.

The testis is just as sensitive to injuries as it is to interruption of its blood supply. As observed from experiments of Kocher, Steiner, Jacobson (223), scars are prone to occur, and atrophy of the whole gland, usually from secondary inflammation, often takes place. An injury of the testis, comparatively very slight, however, is seen in operative incisions. Thus J. E. Schmidt (224) showed in animals, that a testis with such an incision forms only a very superficial scar, of no practical importance. Progressive atrophy does not appear after these operative cuts either in the longitudinal or transverse axis, because the anastomoses are fairly complete.

Many workers have investigated the displacement, and possibilities of *transplantation of the testis* (225). It was found that the organ transplanted in childhood develops in an apparently normal manner at first. But as soon as spermatogenesis begins, involution starts, ending in atrophy. These experimental results correspond with the findings obtained in cases of undescended testicle in man. Thus, in cryptorchitis in the young, the testis is often of normal size, but it is always small and atrophic in adults. Schmidt thinks that pressure changes exerted by the intestines on the testis situated in the abdominal cavity is the cause of this atrophy and he offers, as an interesting proof of his assertion, the fact that in scrotal hernia, the testis is often small and atrophic. In this case a change in pressure from the entering and retreating intestine is present. In a similar way, spermatogenesis is lost, if the testis is transplanted beneath the abdominal skin, even if the vascular supply is perfectly intact. The testis seems to require for its perfect function the loose, half suspended position which it normally occupies. These experimental investigations are of the greatest importance in the treatment of cryptorchism. They show that it is quite indifferent, whether the testicle in cryptorchitis is pushed back into the abdominal cavity or is localized under the skin, spermatogenesis will be lost, while the interstitial cells, and with them the internal secretion, remain intact. But the resistance of spermatogenesis against occlusion of the efferent channels is most remarkable. Posner demonstrated living spermatozoa in the testis after an occlusion of the epididymis or vas deferens for 10 years and more. Thus, theoretically, there is the possibility that removal or short circuiting of the

cicatricially occluded part of the efferent ducts which is practically always due to gonorrhea, will reestablish the emptying of normal semen. Unfortunately, thus far, the practical results have been very poor for technical reasons in spite of the numerous animal experiments, and operations on man (lit. see Schmidt). Probably a successful end has never been reached by implantation of the vas deferens into the testis and similar methods, although Bogoljuboff (226) showed in animals, that such an anastomosis is possible.

### LITERATURE TO KIDNEY

1. Gottstein: Lit. s. Ergebn. d. Chir., V. 2.
2. Lit. see in Volhard: Handbuch d. inneren Med. V. 2.
3. Gross: Ziegler's Beitrage z. pathol. Anat. 51. Baltzner: Mitt. a.d. Grenzgebieten, 1914, V. 28.
4. Richards, A. N.: "Glomerular Function," Am. J. Med. Sci., 1922, 163, 1. Wearn, J. T.: "Observations upon the comp. of glomerular urine," Am. J. Phys. proc., 1922, 59, 490. Cushny, A. R.: "The Secretion of Urine," Monographs Phys. Longmans Green, 1917.
5. Monakow: Deutsch. Arch. f. Klin. Med., V. 102 and 115. Fr. Muller: Verh. d. Deutsch. path. Ges. Merau, 1905.
6. Schlayer: Deutsch. Arch. f. klin. Med., V. 90, 98, 101.
7. Albarran: Exp. des fonct. renales, Paris, 1905.
8. Pflaumer: Schematische Abb. Zeitsch. f. Urol., V. 13.
9. Renner: Arch. f. klin. Med., 1913, V. 110. Smirnow: Anat. Anzeiger, V. 19. Disse: Handbuch d. Anat. by. Bardeleben, 1902, V. 8 und Sitzungsbericht der. Ges. z. Beh. d. ges. Naturwissenschaften, Marburg, 1898.
10. Lobenhof: Mitt. a.d. Grenzgeb., V. 26.
11. Eckhard: Beitr. z. Anat. u. Physiol., 1869-1872, V. 4-9. Jungmann: Jahreskurse f. aerztl. Fortbildung, 1914 and Deutscher Kongr. f. inn. Med., 1913, Kongr. 30.
12. Rohde and Ellinger: Zentralbl. f. Physiol., 1913, V. 27. Asher: Zeitschrift. f. Biologie, 1913, V. 63. (Meyer) Jungmann and Meyer: Arch. f. exp. Path. u. Pharm., 1913, V. 73.
13. Gartani: Arch. ital. de Biol., 1911, V. 56.
14. Kappis: Grenzgebiete, V. 26.
15. Wilms: Munch. Med. Wochenscht., 1904.
16. Lennander: Mitt. a.d. Grenzgebieten, 16.
17. Goetzel and Israel: Pflugers Arch. d. ges. Physiol., V. 83.
18. Adrian: Fol. urolog., 1912, V. 7, p. 95.
19. Masius: cited by Kuster, Chirurgie d. Nieren. Deutsche. Chir., 52, V. 1, p. 55. Cohnheim and Roy: Virchows Arch. V. 92.
20. Ghiron: Berlin. klin. Wochenscht., 1914, p. 158.
21. Meyer and Jungmann: Jahreskurse f. aerzte. Fortbildung, 1914.
22. Jenckel: Deutsche Zeitschft. f. Chir., V. 78.
23. Kapsammer: Nierendagnostik und Nierenchirurgie. Wien., 1902, Wiener klin. Wochenschrift., 1904.
24. Allard: Mitt. a.d. Grenzgebieten, V. 18 (Lit.).

25. Quincke: Arch. f. exp. Pathol. u. Pharmacol, 1893, V. 32.
26. Wiedboltz: Neue Deutsche Chir., V. 6, p. 66.
27. Steyrer: Hoffmeisters Beitrage, 1902, V. 2. Schwarz (Polyuria): Zentralbl. f. Physiol., 1902, V. 2. Allard (Polyuria): Arch. f. exp. Path. u. Pharmac., V. 57. Cohnheim: Allgem. Pathol., V. 2. Ponfick: Zieglers Beitr. z. Path. Anat., V. 49. Pfaundler (Polyuria): Hofmeisters Beitrage, 1902, V. 2. Graser: Chirurgenkongress, 1913. Filehne und Ruschhaupt: Pflugers Archiv., 1903, V. 95. Albarra: Ann. de med. des org. gen., 1907, p. 801.
28. Veil: Bruns Beitrage, 1916, V. 102, p. 367.
29. Pearce: J. Exp. Med., 1908. Passler and Heinecke: Pathologenkongress, 1905. v. Haberer: Mitt. a.d. Grenzgebieten, 1907, V. 17. Bradford: Journ. of Physiol., 1899, V. 23.
30. Veil: Deutsche Arch. f. klin. Med., V. 113, p. 228.
31. Frericks: Die Brightsche Nierenkrankheit Braunschweig, 1851.
32. Reifs: Zeitschft. f. klin. Med., 1914, V. 80. Fr. Muller: Pathologenkongress, 1905. Ascoli: Vorlesungen uber Uraemia, 1903, Jena.
33. Volhard: Handbuch d. inn. med. bei Mohr-Stahelin, V. 3, p. 1314. Lintbeck: Prager. med. Wochenschft., 1892 und Arch. f. exp. Pathol. u. Pharm., V. 30. Strauss: Deutsches Arch. f. klin. Med., 106, Berlin. klin. Wochenschft., 1915. Landois: Die exper. Uraemia, 1888. Pfeiffer: Zeitschft. f. Hyg., 1906, V. 54; Zentralbl. f. d. ges. inn. Med., V. 2, p. 120. Feltz und Ritter: Del' uremie experimentale, Paris, 1881. Bouchard: Lesons sur les antointoxications dous les maladies, Paris, 1887.
34. Heyde and Vogt: Zeitschft. f. d. ges. exp. Med., 1913, V. 1.
35. Gundermann: Munch. med. Wochenschft., 1913.
36. Sauerbruch and Heyde: Ztschft. f. exp. Pathol. u. Therapie, 1909, V. 6.
37. Jehn: Ztschft. f. exp. Pathol. u. Therapie, V. 8. Morpurgo: Pathologenkongress, 1909. Birkenbach (uremia): Ztschft. f. exp. Pathol. u. Therapie, 1909, V. 6.
38. Lindemann: Arch. f. Klin. Med., 1900, V. 65. Koranyi: Koranyi u. Richter, Physikal. Chem. u. Medizin Leipzig, 1908.
39. Traubo: Ges. Beitr. z. Pathol. u. Physiol., 1871, V. 2.
40. Lindemann: Annal. de l' inst. Pasteur, 1900. Tigerstedt and Bergmann: Skandinav. Arch. f. Physiol., 1898, V. 8. Biedl: Innere Sekretion, 2, Edit., 2 V. Brown-Sequard: Compt. rend. de la Soc. de Biol., 1893.
41. Elmendorf: Biochem. Ztschft., 1914, V. 60. Schlayer: Munch. Med. Wochenschft., 1912. Straub: Munch. Med. Wochenschft., 1914.
42. Van Slyke and Collaborators: J. Biol. Chem., 1917, 30, 289. Palmer, W. W. and Van Slyke, D. D.: "Alkali retention and reserve," Journ. Biol. Chem., 1917, 32, 499. Y. Henderson and Haggard, H. W., etc.: J. Biol. Chem., 1918, 33, 333; 1919, 39, 161; 1920, 45, 189; 209, 215.
43. Lennander: Grenzgebiete, V. 10. Harrison: Ref. Munch. med. Wochenschft., 1901, p. 1509. Kummel: Berlin. klin. Wochenschft., 1909.
44. Unger: Chirurgenkongress, 1910.
45. Lit. by Ruge: Ergebn. d. Chirurgie, 1913, V. 6.
46. Zondek: Grenzgebiete, 1907, 3, Suppl. Gawrilow: cited by Latzko, Geb. gyn. Gess. Wien., 1916, Zentralbl. f. Gyn., 1916, p. 599. Biberfeld: Arch. f. Physiol., 1904, V. 102.
47. Zondek: Zeitschft. f. d. ges. exp. Med., 1914, V. 3.
48. Ferrarin: La clinica chirurgica, 1903.

49. Israel, a. o.: Chirurgenkongress, 1904 (discussion).
50. Edebohl: Med. News, 1899; Med. Record, 1901; J. A. M. A., 1907 and 1908.
51. Thelemann: Deutsch. med. Woch., 1902. Zadyier: Grenzgebiet, 14 and 15.  
Fuffier and Ehrhardt: Grenzgebiet, 13. Stursberg: Grenzgebiete, 1903, V. 12.  
Muller: Arch. f. klin. Chir., 82. Parlavocchio: "Le nuove conquiste della  
Chir. Renale," Palermo, 1906. Martini: Arch. f. klin. Chir., 78. Liek:  
Brun's Beit., 1907, 53. Katzenstein: Ztschft. f. exp. Path. and Therapie, 1911,  
9. Bakes: Zentralbl. f. Chir., 1904. Girgloff: Deutsch. Zeitschrift. f. Chir.,  
V. 95. Horchem: Deutsche Ztschrft. f. Chir., V. 93 and Arch. f. klin. Chir., V.  
106. Isobe: Zentralbl. f. Chir., 1907. Asakura: Grenzgebiet, 1903, V. 12.  
Hernheimer and Hall: Virchow's Arch., 1905, 179.
52. Rovsing: Zentralbl. f. Chirurgie, 1904.
53. Gelpke: Korresp.-Bl. f. Schw. Aertzte, 1904. Guiteras: cited by Ruge, Ergebn. d.  
Chir., V. 6. Kummel: Munch. med. Wochenschrift., 1908, p. 587. Baum:  
Munch. med. Wochenschrift, 1908, No. 36.
54. Zondek: Mitth. a.d. Grenzgebieten, 3, Suppl., p. 239.
55. Zondek: Chirurgenkongress, 1899.
56. Albarran: Operat. Chir. d. Harnwege, 1910.
57. See Borst and Enderlen: Deutsche Zeitschft. f. Chir., V. 99.
58. Verlicæ: Compt. rend. Soc. Biol., 1913, V. 75.
59. Menge: Munch. med. Wochenschrift., 1900.
60. Cohn: Zeitschft. f. Urol., 1912, p. 430.
61. Ritter: Chirurgenkongress, 1912.
62. Weissgerber and Perls: Arch. f. exp. Path. u. Pharmak., 1876, V. 6; Arch. f.  
Klin. Med., 1909, V. 97. Buchwald and Litten: Virch. Arch., 1876, V. 64.
63. Isobe: Grenzgebiete, 25.
64. Lit. by Strubell: Der Aderlass. Berlin, 1905.
65. Isobe: Mitt. a.d. Grenzgebieten, 1913, V. 26.
66. Heyde: Chirurgenkongress, 1912.
67. Fiori: Policlinico, 1901, 1903, 1904.
68. Meaugedis: Dis. Paris, 1908.
69. Maas: Deutsche Ztschrift., f. Chir., 1878, V. 10.
70. Kuster: Deutsche Chir. Lief. 52, C. p. 184, ff.
71. Langemak: Deutsche Zeitschft. f. Chir., V. 73. v. Haberer: Grenzgebiete, 1902,  
17. Hermann: Deutsche Ztschft. f. Chir., V. 73. Tillmanns: Virch. Arch.,  
1879, V. 78. Wolff: Die Nierenresection and ihre Folgen, Berlin, 1900. Barth:  
Chirurgenkongress, 1892. Kummel: Naturforscherversammlung Bremen,  
1890. Braatz: Deutsche med. Wochenschrift., 1900.
72. Barth: Habilitationschrift, Berlin, 1892.
73. Wildboltz: Deutsche Zeitschrift., f. Chir., V. 81.
74. Langmak: Brun's Beitrage, 1902, V. 35. Hermann: Deutsche Zeitschft. f. Chir.,  
V. 73.
75. Simon: Brun's Beitrage, V. 59. Simmonds: Munch. Med. Wochenschrift., 1903,  
p. 271.
76. Enderlen: Deutsche Ztschft. f. Chir., V. 41.
77. Wossidlo: Berlin. klin. Wochenschrift., 1914, p. 467.
78. v. Haberer: Arch. f. klin. Chir., V. 86. Schmieden: Deutsche Zeitschft. f. Chir.,  
1903, V. 70.
78. Coenen: Arch. f. Klin. Chir., V. 81.
79. Stoerk: Ziegl. Beitr., 1908, V. 43.



79. Lit. see Rost: (Hypernephroma) Virch. Arch., 1912, V. 208.
80. Nakahara: Virch. Arch., V. 196.
81. Leube: Virch., Arch. V. 72. Furbringer: Zeitschrift. f. klin. Med., V. 1.
82. Senator: Deutsche med. Wochenschrift., 1904, p. 1833 and Die Albuminuria, 1888, 1 edit. Posner: Virch. Arch. Vol., 106.
83. Fischl: Zeitschft. f. exp. Path. u. Therapie, V. 7. Jehle: Ergebn. d. inneren. Med., 1913, V. 12 (lit.).
84. Bauer: Konstitutionelle Disposition zu inneren Krankheiten, 1918, Verlag v. Springer.
85. Bunge: Brun's Beitrage z. klin. Chir., 1919, V. 115.
86. Wunderlich: 3 Wunderlich Pathol. and Therapie, 1856, V. 3. Hildebrand: Deutsche Zeitschft. f. Chir., V. 40. Doll: Munch. med. Wochenschrift., 1907. Coenen: Bruns Beitr., 1910, V. 70. Koch: Deutsche Zeitschft. f. Chir., 1912, 118. Seidel: Chirurgenkongress, 1912. Laewer: Deutsche Zeitschft. f. Chir., V. 113. Baggard: Bruns Beitrage, V. 91. Lenk: Deutsche Zeitschft. f. Chir., V. 102.
87. Ricker: Ziegl. Beitr., 1911, V. 50.
88. Landau: Die Wanderniere der Frau, Berlin, 1881.
89. Kuster: Deutsche Chir. Lief., V. 52, p. 132; compare also Suter in Mohr-Stahlin. Handbuch. d. inn. Med. 2, p. 1754; Kummell in Handb. d. prakt. Chir., V. 4.
90. v. Fischer-Benzon: Dissert Kiel., 1882.
91. Wolkoff and Delitzin: Die Wanderniere, Berlin, 1899.
92. Dietl: Wiener Med. Wochenschrift., 1864.
93. Borzoky: Chirurgenkongress-Zentralbl. 4, p. 323.
94. Riedel: Deutsche med. Wochenschrift., 1907, 41-42. Garre-Eckhardt: Nierenchirurgie, 1907.
95. Hildebrano and Haga 3 (hydronephrosis): Deutsche Zeitschft. f. Chir., V. 49. Tuffier: Annales des maladies des organes genit. urin., 1894.
96. Rautenberg: Mitt. a.d. Grenzgeb., 1906, Vol. 16. Strauss and Gernout: Arch. de Physiol., 1882, p. 386. v. Lichtenberg: Natur. hist. med. Verein. Heidelberg, 1906; Munch. med. Wochenschrift., 1906, No. 32. Posner: Virch. Arch., V. 79. Ponfick: Ziegl. Beitr., V. 49 u. 50. Enderlen: Chirurgenkongress, 1904. Aufrecht: Zentralbl. f. d. med. Wissenschaft., 1870 and 1878. Dunin: Virch. Arch., V. 93.
97. Rost: Munch. med. Wochenschrift., 1919. Levin and Goldschmidt: Virch. Arch. Vol. 134. Haberer Kracke Volker V. Lichtenberg Barbey: cited in Zeitschft. f. urol. Chir., V. 1, p. 567. Kapsammer: 1 Urologenkongress, 1907. Albarran and Guyon: Arch. de med. exp., 1899.
98. Engelmann: Pflugers Arch. V. 2, p. 243.
99. Aksne: Folia urologia, 1908.
100. Enderlen: Munch. Mittheilungen.
101. Stewart and Barbes: Ann. of surgery, 1914, No. 6.
102. Schischko: Chirurgenkongress-Zentralbl., 4, p. 179.
103. Lorin: Chirurgen Kongress-Zentralbl., 4, p. 854.
104. Primbs: Zeitschft. f. urol. Chir., V. 1, p. 600.
105. Kavasoye: Zeitschft. f. gyn. Urol., V. 3.
106. Scott: Chirurgen-Konkress Zentralbl. 3, p. 486.
107. Boetzel: Zieglers Beitr., 1913, V. 57.
108. Voelcker: Chirurgenkongress, 1912.
109. Marcus: Wiener Klin. Wochenschrift., 1903. Lewin and Goldschmidt: Deutsche Med. Wochenschrift., 1897, p. 601-a., No. 52.

110. Wossidlo: Arch. f. Klin. Chir., V. 103; Zeitschft. f. urol, 1917, V. 11.
111. Strassmann: Zeitschft. f. urol. Chir., V. 1.
112. Fr. Muller: Naturforscherversammlung, 1906. Fromme: Verein der Aerzte in Halle Sitzung, 1909, 5, Nov. 10; Munch. Med. Wochenschrift., 1910, p. 327. Cozzolino: cited by Franke, Ergebn. d. Chir., V. 7, p. 705.
113. Hirsch: Dissert. Munchen, 1910.
114. Franke: Mitt. a.d. Grenzgebieten, 1911, V. 22; Berliner klin. Wochenschrift., 1911; Ergebn. d. Chirurgie, V. 7.
115. Scheidmantel: Wurzburger Abhandlungen, 1913, V. 13.
116. Rippert: Deutsche Med. Wochenschrift., 1899. Sittmann: Deutsches Arch. f. Klin. Med., 1894, V. 53. Opitz: Zeitschft. f. Hyg., V. 29. v. Klecki: Arch. f. exp. Path. u. Pharm., V. 39. Pernice and Scagliosi: Deutsche med. Wochenschrift., 1892. Biedl and Kraus: Zeitschr. f. Hyg. u. Infektionskrankheiten, V. 26.
117. Koch: Zeitschrift. f. Hyg. u. Infektionskrankheiten, V. 61.
118. Israel: Chirurg. Klink. der Nierenkrankheiten, Berlin, 1901.
119. Jordan: Chirurgenkongress, 1899-1905.
120. Goppert: Ergebn. d. inn. Med., 1918, V. 2.
121. Sakata: Arch. f. Anat. (u. Physiol.), 1903. Bauereisen: Zeitschrift. f. Gyn. Urol., V. 2.
122. Sagimura: Virch. Arch., V. 206.
123. Lever Stewart: cited in Franke, 114.
124. Selter: Zeitschft. f. Hyg., 1906, V. 54. Rogoszinsky: Zentralbl. f. Chir., 1902, p. 757 (lit.). Conradi: Munch. med. Wochenschrift., 1909, p. 1318. Cohn: Berliner klin. Wochenschrift., 1900. Hornemann: Zeitschft. f. Hyg, 69.
125. Wasserthal, Epstein: Berlin. kl. Wochenschrift., 1909. Roubitschek: Berliner klin. Wochenschrift, 1910.
126. Brunn: Arch. fr. Klin. Chir., V. 65.
127. Wreden: Zentralbl. f. Chir., 1893.
128. Faltin: Zentralbl. f. d. Krankh. d. Harn and Sexualorgans, V. 12.
129. Posner and Lewin: Zentralbl. f. d. Krankheiten d. Harn u. Sexualorgans, V. 7.
130. Marcus: Wiener klin. Wochenschrift, 1901, No. 1.
131. Biedl and Kraus: Arch. f. exp. Path. u. Pharm. 3.
132. Lewin: Arch. f. exp. Path. u. Pharm., V. 40. v. Wunschheim: Zeitschft. f. Heilkunde, V. 15. Marcus: Wiener Klin. Wochenschrift., 1903. Schmidt-Aschoff: Pyelonephritis in anat. u. bakt. Beziehung, Jena, 1893. Savo: Wiener Klin. Wochenschrift., 1894. Albarran: These de Paris, 1889.
133. A. Muller: Arch. f. Klin. Chir., 1912, V. 97.
134. Bertelsmann and Man: cited by Suter von Mohr-Stahelinschen-Handbuch, 3, p. 1768
135. Paranephritic Abscesses. Lit by Wurster: Diss. Wurzburg, 1910.
136. Kummell: Handbuch d. prakt. Chir., V. 4, p. 514.
137. Lit. see Frank: Zentralbl. f. d. Grenzgebiete, V. 14.
138. Foulerton and Hillier: Brit. med. Journ., 1901. Kiellcuthner: Fol. urol., 1912, V. 7. Rolly: Munchener med. Wochenschrift., 1907. Jousset: Arch. med. exp., 1904.
139. Seeliger: Zeitschft. f. Urol., 1909. Orth: Berlin. klin. Wochenschrift., 1907.
140. Kuster: Chirurgie d. Nieren. Deutsche Chir.
141. Meinertz: Virch. Arch., V. 192. Hansen: Annal. des. mal. des org. gen-urin., 1903.

142. Pels Leusden: Arch. f. klin. Chir., V. 95.
143. Albarran: Assoc. franc. d. urol., 1904.
144. Tendeloo: Munch. med. Wochenscht., 1905.
145. Guyon: Lecons cliniques sur les maladies des voies urinaires, Paris.
146. Baumgarten: Arch. f. Klin. Chir., V. 63, p. 1019. Sawamura: Deutsche Zeitschft. f. Chir., 1910, V. 103.
147. Bernard and Salomon: Compt. rend. de la soc. de biol., 1905. Kappis: Arb. a. d. Gebiete d. pathol. Anat. u. Bacteriol. Tubingen, 1906.
148. Rovsing: Zeitschft. f. Urol., 1909, Vol. 3.
149. Simmonds: Deutsche med. Wochenscht., 1915.
150. Voelcker: Lit. see Voelcker, Chir. d. Samenblasen, Neue Deutsche Chir., V. 2.
151. Kramer: Arb. auf. d. Gebiete d. pathol. Anat. u. Bakt., V. 4 u. Kramer: Deutsche Zeitschft. f. Chir., 1903, V. 69.
152. Teutschlander: Beitr. z. Klinik. d. Tuberculose, 1906, V. 3 and 5.
153. Loeb: Diss. Giessen, 1866.
154. Oppenheim und Loew: Virch. Arch., V. 182.
155. Baumgarten: Berlin. Klin. Wochenscht., 1905.
156. Janis and Nakarais: Zeitschft. f. Urol., 1909, V. 3, p. 712.
157. Dette Santi: cited in Handb. d. prakt. Chir., V. 6, p. 1064.
158. Treindlsberger Schlagintiveit: Deutsche Ges. f. Urol. 4, Kongr., 1913; Beiheft d. Zeitschr. f. Urologie, 1914. Hirsch: Historisch-geograph. Pathologie, 1886, V. 3, Stuttgart.
159. Kuttner: Bruns Beitrage, V. 63.
160. Condrey: Journ. d' urol., 1913.
161. Goebel: Ergeb. d. Chirurgie, V. 3.
162. Osborne, T. B., Mendel, L. B. and Ferry, E. L.: J. A. M. A., 1917, 49, 32.
163. Schade: Munch. Med. Wochenscht., 1909, 1 u. 2, 1911, Med. Klin. Lichtwitz: Zeitschft. f. Urol., 1913.
164. Kleinschmidt: Die Harnsteine Berlin Springer, 1911.
165. Posner: Deutsche Ges. f. Urol. 4 Kongr., 1913 (disc.). Brugsch: Klemperer Munchener med. Wochenschrift, 1908.
166. Ebstein: Deutsche Zeitschrift. f. Chir., V. 7.
167. Studensky: Deutsche med. Wochenschrift, 1908, No. 32 (literature).
168. Quincke: Deutsches Arch. f. Klin. Med., 1902, V. 9.
169. Nicolaier and Ebstein: Exper. Erzeugung von Harnsteinen Wiesbaden, 1891.
170. Rosenbach: Mitth. a. d. Grenzgebieten, 1911, V. 22.
171. Langendorff and Mommsen: Virch. Arch., 1877, V. 69.
172. Posner: Zeitschft. f. klin. Med., V. 16. Pfeifer: Verhandl. d. Kongr. f. inn. Med., 1886.
173. Kahn: Arch. of int. med., 1913, V. 11.
174. Kumita: Mitteil. a. d. Grenzgebieten, 1909, V. 20.
175. Klauser: Bruns Beitrage, 1914, V. 94, p. 98.
176. S. v. Zeissl: Pflugers Arch., V. 53, 55, 89. Rehfish: Virch. Arch., V. 150. v. Frankl-Hochwart-Zuckermandl: Nothnagels Handbuch Lief., 1906, 19. Muller: Deutsche Zeitschft. f. Nervenheilkunde, 1902, V. 21 u. Deutsch. Arch. f. klin. Med., 1918, V. 128. Frohlich u. Meyer: Wiener klin. Wochenschrift, 1912. Rost: Munchener med. Wochenschrift, 1918, No. 1. Langley: Journ. of physiol., V. 29. Elliot: ibid., V. 35. Schwarz: Mitt. aus d. Grenzgeb., 1917, V. 29. Metzner: in Nagels Handbuch d. Physiologie, Adler. Grenzgebiete, V. 30. Debaisieux: Chirurgenkongress-Zentralbl., 2, p. 278.

177. S. also the schematic illustr. of Pflaumer Zeitschr. f. Urol., V. 13.
178. Homburger: Therapie d. Gegenwart, 1903.
179. Karplus und Kreidl: Arch. f. Physiol., 135.
180. R. Zimmermann: Mitt. a. d. Grenzgebieten, V. 20, p. 455. Muller: Mitt. a. d. Grenzgebieten, V. 18, p. 633.
181. Posner: Diagnostik und Therapie d. Harnkrankheiten, Berlin, 1894. Finger: Wiener allg. med. Ztg., V. 38.
182. Frohlich and H. H. Meyer: Wiener klin. Wochenschr., 1912, No. 1.
183. Rost: Munchener med. Wochenschrift, 1918, No. 1.
184. Schwarz: Mittheil. a. d. Grenzgebieten, V. 29. Adler: Mitt. a. d. Grenzgebieten, V. 30.
185. Treskin: Pflugers Arch., V. 5. Mass and Pinner: Deutsche Zeitschr. f. Chir., V. 14.
186. Rovsing: Klin. and exper. Untersuchungen uber die infek. Erkrankungen d. Harnwege, Berlin, 1898. Melchior-Suter, a. o.: Zeitschr. f. Urol., V. 1 (lit.).
187. Strauss: Zeitschr. f. Urol., 1919, V. 13.
188. Bumm: cited by Stoeckel Handbuch d. prakt. Chir., V. 4, p. 843, 4 edit.
189. Leube: Virch. Arch., V. 100.
190. Freudenberg: Munch. med. Wochenschr., 1918, p. 277, disc.
191. Leueberger: Bruns Beitrage, V. 80, lit. Rehn: Arch. f. klin. Chir., V. 50. Oppenheimer: Munch. med. Wochenschr., 1920, No. 1.
192. Wallney: Diss. Greifswald, 1866. Ullmann: Wiener med. Wochenschrift., 1887. Rivington: Lancet, 1882. Stubenrauch: Arch. f. klin. Chir., V. 51. Dittell: Wiener med. Wochenschr., 1886. Bartel: Arch. f. klin. Chir., V. 22. Brand: Arch. f. klin. Chir., V. 55. v. Beck: Deutsche Zeitschrift. f. Chir., 19. Howell: These de Paris, 1857.
193. Rost: Munchener med. Wochenschr., 1917. Oehlecker: Deutsche med. Wochenschr., 1912.
194. Virgli: Chirurgenkongress-Zentralbl., 4.
195. Nagano: Bruns Beitrage, V. 38. v. Brunn: Deutsche Zeitschrift. f. Chir., V. 73. Enderlen: Deutsche Zeitschrift. f. Chir., V. 55.
196. Ingianni: Deutsche Zeitschr. f. klin. Chir., 1900, V. 54.
197. Rehfish: Virch. Arch., 1897, V. 150.
198. Lendorf: Arch. f. klin. Chir., 1912, V. 97.
199. Frisch: see Frisch im. Handbuch d. Urol. heraus g. v. Frisch Zuckerkandl. Hirt. Ergebn. d. Chir., V. 1; Schlange im Handbuch d. prakt. Chir., V. 4.
200. Rothschild: Fol. urol. Deutsche med. Wochenschr., 1909, No. 33. Runge: Mitt. a. d. Grenzgebieten, V. 20.
201. Marion: Fol. urol., V. 5. Loeschke Naturhist. med. Verein. Heidelberg, 1919. Lendorf: Arch. f. klin. Chir., 97, p. 467.
202. Reerink: Deutsch. Chirurgenkongress, 1903-1904.
203. De Quervain: Chirurgische Diagnostik., F. C. W. Vogel, Leipzig, 3 Edit., p. 429.
204. Wilms: Munchener med. Wochenschrift, 1916. Schlange: Handbuch d. prakt. Chir., V. 4.
205. Rovsing: 36th Chirurgenkongress. Grunert: Munchener med. Wochenschr., 1907. Koenig: Munchener med. Wochenschr., 1906.
206. Furbringer: Nothnagel's Handbuch d. inn. Med., V. 19.
207. cf. Biedl: Innere Sekretion, 2 Edit. 2 part, p. 341.
208. Wilms-Posner: Munchener med. Wochenschr., 1911, No. 36.
209. v. Bramann-Rammstedt: Handbuch d. prakt. Chir., V. 4, p. 1066, 4 edit.



210. Lichtenstern: Munch. med. Wochenschrift., 1916, No. 19.
211. Tandler and Gross: Arch. f. Entwicklungsmech, 27, 29, 30 and Wiener klin. Wochenschrift., 1907, 1908, 1910.
212. Steinach: Pflugers Archiv., 1894, V. 56; Zentralbl. f. Physiol., V. 24 u. 27.
213. Rohleder: Deutsche med. Wochenschrift., 1917.
214. Frankl-Hochwart: Wiener med. Wochenschrift, 1910.
215. Melchior: Lit. Ergebn. d. Chir., V. 3. v. Eiselsberg: Wiener klin. Wochenschrift., 1907. Horsley: Brit. med. journ., 1906. Hochenegg: Chirurgenkongress, 1908.
216. Frohlich: Wiener klin. Rundschau, 1901. Bartels: Zeitschft. f. d. Augenheilk, 1906, V. 16.
217. Madelung: Arch. f. Klin. Chir., V. 73, p. 1066.
218. Cushing: J. A. M. A., 1909, V. 53, p. 249.
219. Frank: Berliner klin. Wochenschrift, 1910.
220. Simmonds: Munchener med. Wochenschrift., 1913, p. 127.
221. Tandler: Arz. d. Wiener Akad., 1910.
222. Tomsa: Jahresbericht d. Ak. d. Wissenschaften, 1862, Wien., V. 46. Miflet: Arch. f. klin. Chir., 24. Enderlen: Deutsche Zeitschft. f. Chir., V. 43.
223. Steiner: Arch. f. Klin. Chir., V. 16, p. 187. Jacobson: Virch. Arch. 75, p. 349.
224. J. E. Schmidt: Bruns Beitrage, 1912, V. 82.
225. Posner: Berliner klin. Wochenschrift., 1905. Stilling: Ziegl. Beitr., 1894, V. 15. Matsuoka: Virch. Arch., 1903, V. 18c. Steinach: Zentralbl. f. Physiol., 1910, V. 24. Hanau: Pflugers Arch., 1897, V. 65. Goebell: Zentralbl. f. Path., 1898. Berthold: Arch. f. Anat., 1849.
226. Bogoljuboff: Arch. f. klin. Chir., V. 70 and 72.

## CHAPTER IX

### THE THYROID GLAND

The attitude with which surgery has regarded the thyroid gland and its diseases has undergone a tremendous change in the last few decades, and the many surgical operations on the thyroid have contributed not a little toward directing our knowledge of the normal and the pathological physiology of this organ into the proper channels.

In the beginning, it was chiefly the mechanical interference with breathing and circulation from enlargements of the thyroid, "goiter," which led to operative interference. For cosmetic reasons, also, removal was desired. At first, the gland was usually removed in toto, but it was soon observed (1) that grave general disturbances followed this procedure (cachexia strumipriva, or thyreopriva). These unlooked-for occurrences showed that the thyroid has an important place in the economy of the body, one which should be investigated and analysed (2).

The older views concerning the *functions of the thyroid* are admirably discussed by Horsley (3) in the dedicatory volume to Virchow. Now, it can be definitely said that the thyroid is chiefly an organ of internal secretion even though the actual secretion has not as yet been demonstrated in the venous blood leaving the gland. Since ligation of all the veins leads to red infarction, this procedure is ineffectual in deciding the question of whether the secretion leaves by way of the blood or the lymph channels (4). From the gland substance itself, Baumann (5) isolated iodothyryn, an iodine-containing protein, which according to the investigations of Oswald (6) is only a decomposition product, while the actual secretion is iodothyreoglobulin, also an iodine-containing protein. According to the latter, this iodothyreoglobulin "possesses all the physiological peculiarities of the thyroid gland itself," which is not true of the iodothyryn (7). Thus it favorably influences the cachexia strumipriva following extirpation as well as the myxedema of adults which results from failure of function. Furthermore, it increases the general oxidative processes of the body and acts on cardiac and vasomotor nerves. Finally, according to Koch (6), it increases the resistance of the body to methylcyanide, and has, therefore, a detoxifying activity also. In addition to the iodothyreoglobulin, cholin was found and a nucleoprotein was isolated (Oswald), which together with the iodothyreoglobulin represents the colloid of the anatomists. That the symptoms exhibited in man and ani-

mals in whom the thyroid has been removed or is functionless, are made to disappear in greater or less degree by the administration of iodothyroglobulin indicates that the most obvious function of the thyroid is to secrete this substance, but the possibility that it has other duties to perform should not be entirely forgotten.

[Kendall's isolation of a substance from the thyroid to which he has given the name "thyroxin" probably marks the final step in the purification of the active principle of the gland. As is well known, it has the physiological activities of the dried gland itself (8).]

It has been mentioned that the thyroid was suspected of having some sort of detoxifying action (9) and it is possible that those manifestations, which are regarded as the result of extirpation of the gland, may be a poisoning by substances which ordinarily are rendered harmless. Undoubtedly, this question is extraordinarily complicated. It is known that thyroidectomized animals have little resistance to certain inorganic poisons such as bichloride of mercury (10). But on the other hand, Gottlieb (11) showed that such animals actually have an increased resistance to poisoning by morphine because they are better able to decompose it.

Reid Hunt (12) found that white mice which had been fed with thyroid substance could withstand much better than normal animals acetonitril which acts as a cyanide in the body. He, however, does not conclude that these experiments show a detoxifying function of the thyroid. Trendelenburg (13) believes such a power is indicated by experimental results from somewhat different methods. He fed his white mice, not with thyroid substance, but with the blood of thyroidectomized cats. These mice were also able to withstand acetonitril better than the controls. Trendelenburg believes that there are substances in the blood of thyroidectomized animals which may be regarded as toxic products of cell metabolism and that normally these are collected by the thyroid and rendered harmless. If this conclusion is to be adopted, however, it would be necessary that the blood of these cats contain lasting and always increasing amounts of these substances. This was not the case in Trendelenburg's experiments, the results were positive only when the blood was taken from 48 to 72 hours after the glands were extirpated. It must be admitted that none of the experiments to date have sufficiently proven that the symptoms following thyroidectomy can be regarded wholly or in part as the result of "poisoning" with substances which the thyroid normally destroys. The possibility, of course, should not be entirely forgotten.

Investigations (14) have shown that changes in the sense of chronic or subacute inflammatory processes are found in the thyroid in infections

and intoxications, but how far the term "function" may be applied in these conditions is not as yet known.

Still less supported are other theories of the functional importance of the thyroid, particularly the one which regards it as a regulator of the blood supply of the brain. Some theories, such as its importance in blood formation and in the development of the sexual organs, can be explained sufficiently from the standpoint of internal secretion. They are undoubtedly based on correct observation, but the interpretation is usually somewhat one-sided.

The *nerve influencing secretion* is the superior laryngeal. This was prettily demonstrated in the experiments of Asher and Flack (15) in which they found that stimulation increased the irritability of the vagus and depressor nerves, which otherwise occurs only after the injection of thyroid substance, moreover, these experiments are the only ones up to the present, which offer direct proof that thyroid secretion normally enters the blood stream. The rich nerve supply of the thyroid is shown in the anatomical investigations of Andreson (16).

Even if it is assumed that the thyroid gives its secretion direct to the blood, it is still difficult to understand the manner in which it produces *its effects on the body*, for it increases the function of one organ and inhibits that of another, which facts point to an indirect rather than a direct action. The thought of some sort of a ferment has occurred. Mikulicz has used the pithy term "multiplier," which means that this substance increases the general irritability and metabolism of the body. It is not known whether the effect is exerted through the nervous system or on the body cells themselves.

It was the *effect of total thyroid extirpation* which was the principal stimulus to interest in the functions of the gland. The acute symptoms (tetany) are, of course, as later experiments showed, results of the removal of the parathyroids. A chronic cachexia thyreopriva is the only effect which can be considered due to thyroidectomy (1). The symptoms in children and adults are not entirely identical. In the former there are disturbances in growth and the general body development; the growth in height is particularly interfered with by defective ossification of the epiphyses; the genital organs remain small; puberty, if it occurs at all, is late. After extirpation of the gland in adults, menorrhagia in women and impotence or sterility in men have been observed. The skin manifestations are peculiar and similar in all cases. It becomes doughy and edematous, and pale in color. Eppinger (17) showed that physiological saline solution is absorbed more slowly from the subcutaneous tissues in myxedema, but the cause of their dough-like consistency is not definitely known. A difference in the ability to distend has been spoken of (Biedl



10, p. 165). The hair becomes prematurely gray, dries and falls out. The general metabolism is decreased, the appetite is poor. In the beginning, according to the studies of v. Bergmann (18), there is an increase in weight, since there is a positive nitrogen balance. Gradually, loss of weight follows with progressive emaciation and weakness, and death occurs not later than seven years after operation. At the same time there is a pronounced decrease of intelligence, and the patients gradually become total idiots. At autopsy, in addition to the emaciation, etc. the hypophysis is found enlarged from increase in the cellular elements and from hyperemia (19). This is found so consistently after failure of the thyroid that it indicates some relation between these two glands. In regard to the other endocrine organs, there is a decreased weight of the thymus in addition to the diminution in size of the genitalia.

Animal experiments designed to study the effects of thyroidectomy give the same general results as in operative human cases (10), (20). In such experiments, it is better to use herbivorous animals because the parathyroids of carnivora are in such intimate contact with the thyroid that it is very difficult to remove it completely, without injuring or removing the parathyroids (10), (21). But when the operation is successful, the results in carnivora are quite similar to those in herbivora with differences only in the details. Thus Biedl's dogs showed very large thymus glands at autopsy while it is usually found diminished in size, as stated before. Furthermore, no psychical changes were observed in dogs, but these appear in herbivora just as in man. Young animals show disturbances of the growth in length similar to those in humans. The blood picture in both man and animals shows a decrease of erythrocytes and of hemoglobin and a coincident leucocytosis (22). Blood coagulation is delayed at first, but later the formation of coagula is abundant, with the fibrin apparently increased (10). These changes, suggestive of metabolic disturbances, have not been explained.

With the removal of the thyroid in the young not only is the bone growth changed, but cellular growth in general becomes somewhat sluggish. Fractures heal more slowly and the formation of callus as well as the reabsorption of it, is delayed (23). Marinesco and Minea and F. H. Walther (24) observed a markedly delayed degeneration and regeneration in cut nerves. Ordinary wounds in soft parts are supposed to heal more slowly (25). Furthermore, it has been found that certain disturbances occur in other internal secretory glands, as in the pancreas and in the chromaffin system; but these questions are still in the formative stage (26).

The pure form of results and after effects of thyroidectomy are seen best in experimental removal of the gland and after the radical operation in man, for in the diseases considered sequellæ of the failure of thyroid

secretion, there is always a complicated symptomatology because the lengthy absence of the thyroid brings into involvement other organs, especially the endocrine glands. Of the diseases which we relate to the absence of thyroid secretion, *myxedema* must be named first. In both cases, although the thyroid is absent or much atrophied, a differentiation between that of adults and the congenital type must be made. The clinical symptoms correspond perfectly with those of experimental thyroidectomy. In children who are perfectly normal at birth and in whom the symptoms develop with increasing age, the predominant signs are mental dullness and defective bony development. In adults, the increasing dullness of intellect, and idiocy are the most prominent signs. Less severe cases often begin with lassitude and somnolence and mental inability. That all of these clinical symptoms result from the abolition or decrease of thyroid function is proven by the fact that the myxedema of adults is practically certain to improve or disappear after treatment with thyroid substance or by implantation of the gland (27). But the results of thyroid implantation in animals are not quite uniform. Enderlen (28) believes that the supply of colloid from the implanted gland is insufficient, while Cristiani arrived at an opposite opinion and proved with Kummer that these glands actually enlarge and form a kind of new thyroid.

In the myxedema of children the results are less satisfactory, which is due, according to the general view, to the marked involvement of the other endocrine glands which has taken place previous to the time treatment is begun. Indeed, it is quite possible that the myxedema of children is not merely a result of the absence of the thyroid, but that primarily other ductless glands are defective. First of all, absence or insufficiency of the thymus gland must be considered, because not only is the clinical course markedly different from that in adults, and from cachexia thyreopriva, but it shows many analogies to experimental thymus extirpation (29).

Another disease complex considered due to thyroid insufficiency is *endemic cretinism* (30). By this is understood a mental deficiency disease of endemic form, with body changes corresponding to those described in myxedema. But cretinism is differentiated from myxedema by the fact that it is practically always, or in the majority of cases accompanied by goiter, and for this reason the problem is closely bound up with the goiter problem, and often simply identified with it. To what extent this is justified by our present knowledge, will be discussed later. Further marked differences between myxedema and cretinism can be found in the progressive character of myxedema, leading finally to death, while the cretin lives to a practically normal age. The retardation of bone growth also shows differences in the two diseases. In cretinism, it is irregular

with both a delay in bone building, and a premature ossification (Ewald (30)). That the thyroid function is defective in the myxedema of adults as well as in cretinism, is shown by the improvement in both diseases after treatment with the extract. Of course, this does not prove that the thyroid gland is necessarily the most essential factor in this pathological-physiological process; this can be stated positively only when we acquire better knowledge of the etiology of both diseases. Kutschera (27) classes as cretinism everything of a physical and mental underdevelopment which appears in the endemic area and is caused by the cretinogenic "influence," justifying his viewpoint, from the fact that various disturbances in the endemic area are often simultaneous, especially in children of one family. He also emphasizes that cretinism does not exist without goiter, which is recognized now by practically all authors. But there is also an injury of the nervous system which probably is not dependent on the goiter, but is of equal importance. According to Kutschera again, the condition might possibly be an injury, arising from an infection, which acts primarily on the nervous system and this in its turn compels the thyroid gland to produce less secretion. This defective function may now produce new injuries to the nervous system and so on.

At any rate, these statements show that goiter and cretinism are closely related. Or with reservations, a certain type of goiter must be etiologically considered together with cretinism, but whether the statements regarding its etiology hold good in the other goiters to be discussed, is difficult to say at present. The goiter problem has been approached thus far from only the endemic viewpoint and it remains an open question whether other goiters have a different etiology.

Practically everything known in general pathology as a cause of disease, has been held responsible for the development of *goiter*, a sure sign that our actual knowledge in this matter is very meager. The difficulties begin when even a definition of goiter is attempted. It is, of course, generally understood that this implies an enlargement of the thyroid, and naturally that all pathological anatomical details are carefully investigated. But even, if we wish to draw conclusions of the type of anatomical and functional change in a gland from its microscopical preparation, insuperable difficulties are encountered, consisting chiefly of our inability to recognize the route and the degree of excretion from the gland. We cannot say whether an increased formation of secretion or excretion takes place, or if it is stored up; in other words, we do not know whether the picture in a given case is an expression of hyperfunction, or should be interpreted in the sense of tumor formation. In all probability we will not progress very far until the etiology becomes clear. The solution of this question is paramount. The pursuit has been along two roads,



*viz.*, the production of goiters experimentally, and the study of their epidemiology.

It is an ancient belief, shared by Hippocrates, that the drinking of water from certain wells caused goiter, but only recently have attempts been made to verify this by animal experimentation (31). At first, results seemed successful, but the more numerous the investigations, the more evident it became that conditions were far more complicated than had been imagined. In the first place, it was found that in those regions where goiter is endemic, animals develop them spontaneously. Experimental results obtained in these geographical localities cannot, therefore, be accepted without reservation. Animals kept there often showed actual endemics, although they received untainted water (for instance in Zurich). It was found that some of these animals occupied quarters formerly occupied by goitrous animals, and, moreover, that a newly arrived animal with goiter, "infected" the whole kennel. Possibly the lack of cleanliness and food soiled with feces (Bircher (31)) might have been the cause of such transmission, but control investigations proved that this conclusion was also erroneous. Grassi and Munason (10) kept their dogs in cages cleansed daily with disinfectants. The food and water was sterilized, but since they experimented in goiter regions, their animals developed enormous goiters. The same experiments undertaken in goiter free regions not only gave negative results, but showed that imported goitrous animals became goiter free. This is observed in man quite often. Furthermore, the fact that no goiter developed in animals if a trace of iodine was added to their water, gave rise to the belief that the lack of iodine caused goiter formation, but neither this theory nor similar ones suggesting special chemical properties of goiter water, could be proven.

Epidemiological investigations have given no better support to the "water-theory." These were made chiefly by H. Bircher (32) who because of its prevalence in Switzerland supported the opinion that goiter was related to special geological formations. Supposedly it does not occur in volcanic formations, jura or chalk, or in rain water deposits, but is found with marine sediments of the palæozoic, trias and tertiary ages. Kocher (33) pointed out that this classification could not be strictly maintained. Some authors such as Lobenhofer (34) thought they could strengthen Bircher's theory by investigations in other goiter areas. But Hesse found that goiter free inhabitants in Switzerland lived among the same rock formations as those in Saxony who had much goiter, and *vice versa* (35). Bircher's view, therefore, has no general value. Schittenhelm and Weichardt (36) also found that in Bavaria similar geological formations sometimes show goiter and sometimes not. Furthermore, the very accurate reinvestigations of Dieterle, Hirschfeld and Klinger (37) over the same territory



investigated by Bircher, could not prove that the presence of goiter depends on such geological formations and their differences, when all of the population was examined. Furthermore, Bircher's evidence for the water theory in a mass experiment which consisted of showing that a locality completely filled with goiter, became goiter free after switching the water supply from one to another geological formation, could not be confirmed by these re-investigations. It was found that part of this new water supply did not have its origin in primeval rocks, but came from marine deposits. Finally, a careful examination of all the population showed that the decrease of goiter in these localities was by no means as remarkable as it appeared from the military draft lists.

Kutschera (27) working in Styria found that although certain houses were supplied by water from the same source, some of their inhabitants had goiter, and others none. He could also show how little the water theory applies, by other very interesting examples, as for instance, in his investigations of the "Tostenhuben" in Karnten. These are isolated houses in which, according to century old history (v. Fradeneck), all children and adults were cretins, having goiter also. Kutschera found that two of these Tostenhuben which had burned down in the meantime, and were rebuilt, harbored no more cretins. In one, it could be shown that a child born before the fire was a cretin, while all children born afterwards were normally developed. From a third, goiter disappeared after it had remained empty for 40 years. In all these cases the water supply had always remained the same. From those and other investigations carried out with remarkable accuracy Kutschera concluded, probably correctly, that goiter depends not on the water supply but on the social community, in other words, that it must imply infection from man to man, but from very close contact. Kutschera offers very interesting leads to this thought; for instance, Kostel reports that in former times the nobility in Wallis raised only their first born at home, and intentionally turned over the children born later to their cretin servants that these younger children might become cretins, and thus prevent scattering of the property. If children born of a cretin mother were removed and raised in a goiter free neighbor's home, they developed normally. Kutschera could bring proof of his opinion even in animal experiments. He observed that a cretinous village pauper had great affection for dogs. Those dogs slept with her in a filthy bed consisting only of woolen rags, and were pronounced cretins. Kutschera took these dogs from the woman, giving her successively, several healthy young dogs to be cared for. These latter eventually became cretins and developed goiters. The rest of the same litter, which he kept himself, were normal.

Unquestionably these careful investigations of Kutschera strengthen

the theory that goiter is an infectious disease, but no infectious factor has been demonstrated. Naturally, even less can be said of the place and mode of entrance of the infection. All statements, for instance, that infection arose in the intestines somewhat like the formation of a toxin, which the thyroid gland supposedly detoxified, or that it was only from a special mixture of intestinal bacteria, possibly influenced by special food, are still in the clouds. In Brazil, a trypanosome has been discovered as the cause of a special type of goiter (Chaga's disease).

Oswald's finding, that in 84 per cent. of the inhabitants of Switzerland, the thyroid gland has a greater weight than in regions free from goiter, will doubtless be of future value in the etiological study of the goiter problem. At present it cannot be properly interpreted.

Mansfeld and Fr. Muller (38) concluded that a deficient oxygen supply may result in a functional change in the thyroid, because they found a decreased nitrogen elimination in rabbits which had been thyroidectomized and permitted to breathe for some time, in an atmosphere of diminished oxygen content. Normal rabbits, breathing the same atmosphere, conversely, showed increased nitrogen elimination. Surgically, these experiments are interesting since it might be concluded that mechanical obstruction to respiration, *e.g.*, goiter, would suffice to stimulate hyperfunction of the thyroid gland. But the work of Reich and Blauel (39), who produced tracheal stenosis in rats, has shown that such stenosis, on the contrary, leads to degenerative processes in the thyroid, and these experiments seem to justify the assumption that hypofunction and not hyperfunction is a result of respiratory resistance as we find it in goiter. Differences in thyroid function would occur according to the length of time respiration has been impeded.

In contradistinction to diseases caused by hypofunction of the thyroid gland, are those which have recently been considered as due to excessive function, or *hyperthyroidism* (40). It is still undecided whether the disease complexes differentiated in this discussion are actually different forms, or only stages of one and the same disease, but knowledge of them has been considerably increased by operative treatment. The surgical point of view has been influenced by both the operative improvement in large numbers of cases of Basedow's disease, and by the poor operative results in other cases; and finally, by the sudden death which sometimes occurs after operation. The beneficial results seemed to offer proof for the correctness of the theory of hyperthyroidism. The poor results and the deaths taught us that the problem is far more complex than was imagined.

If we attempt to begin our study from the results of experiment, we find that little has been discovered (41). A healthy individual or an

animal may be fed with thyroid gland without developing exophthalmic goiter. In the common, and in the endemic goiter also, thyroid feeding leads very rarely to actual hyperthyroidism. Only one symptom appears at all consistently in these feeding and injection experiments and that is tachycardia. Iodine is more dangerous, if fed or injected, than thyroid gland-juice itself (42). It is often used in goiter, but it was found that this medication frequently leads to the disease complex usually called thyroidism, the chief symptoms of which are palpitation of the heart, tachycardia and general nervous excitement; furthermore it results in a decrease of the lymphocytes. Since surgeons show a tendency to consider these conditions as mild or incomplete forms of Basedow's disease, it is sometimes spoken of as an "iodine Basedow's" (43).

[The experimental work which has been performed with iodine has led to the brilliant results of Marine and his coworkers in the prevention of simple goiter in man. Working with the school children in Akron, Ohio, many of whom were either beginning to have, or would have developed goiter according to the probabilities, they succeeded in not only reducing the ordinary incidence to practically negligible numbers, but in actually causing the goiter to disappear in one-third of the already developed uncomplicated cases. The method is simple and consists merely in giving 2 grams of sodium iodide in small doses, twice yearly, at the age of puberty. The prevention of fetal and maternal thyroid enlargements may be accomplished in a similar manner. The authors suggest that the first problem is essentially one of the public health, while the second more properly is a responsibility of individual physicians (44).]

The action of iodine presumably causes an increased secretion of the gland, but we have no direct proof for this belief. At any rate, it must be emphasized especially that healthy individuals, and as stated, many people with endemic goiter, do not react in this manner to iodine, but that it is always single special types which develop these symptoms. This proves, just as the results of thyroid feeding, that, even if we assume that the gland increases its secretion for which, as must again be emphasized, we have only indirect proof, some sort of a second factor must be present if exophthalmus or thyroidism is to develop. The supposition of a hypersecretion in view of the facts of experiment, does not suffice to explain the disease picture. The assumption was first made, principally through clinical observations, that exophthalmic goiter and related disease symptoms, depend on increased secretion of thyroid gland tissue. Mobius (40) pointed out that there is a sharp distinction between myxedema and Basedow's disease which can be followed in all details, and it was natural, with this contrast in the disease picture, to look for a contrast in the

etiology. Since it was recognized that myxedema is produced by a failure of the thyroid, Modius supposed that Basedow's disease and related symptoms are due to excess of thyroid secretion. His theory seemed to be much strengthened by the results of operative removal. But it was not overlooked that quite a percentage of these patients were not cured or that only some symptoms were relieved even though considerable tissue was removed.

Then it was assumed that the secretion was not merely excessive, but it entered the circulation in a changed form. The most varied investigations have been undertaken to demonstrate such a "dysthyroidism" (45), (40). The first procedure was to inject animals with the fluid expressed from the goiters of Basedow's disease and although isolated, positive results were obtained, none of the workers could produce a typical Basedow's disease, but only a few somewhat characteristic symptoms. According to Furth (41) tachycardia is the most constant symptom in hyperthyroidized animals. But the majority of the authors using similar experimental methods, observed only general symptoms of intoxication (43), (46). Klose, reporting experiments with dogs which had been in-bred for a long time and thus degenerated (fox-terriers), succeeded in inducing a typical Basedow's disease with exophthalmus and tachycardia, by the injection of the pressed juice of extirpated exophthalmic goiter tissue. But Baruch (47) was not able to verify these findings. The results of Klose's investigations have been interpreted with due care, but it is really very difficult to judge in an animal, whether symptoms are present which correspond to Basedow's disease in man, and if the dogs did develop a true Basedow's the statement of Oswald cannot be ignored, *viz.*, that the result was achieved in degenerate dogs, perhaps as in humans, who react to iodine and increase of thyroid secretion with exophthalmic goiter. They may in some way have been predisposed to the disease. Oswald (6) also challenged the investigations of Walther and Hosemann (48) who believed that the thyroid gland of exophthalmic goiter contains a specific secretion, because nerve regeneration can be stimulated in thyroidectomized animals with the juice of the ordinary thyroid gland, but not with that of exophthalmic goiter. In such examinations it must first be proved that a similar quantity of iodothyreoglobulin [(thyroxin)] is present in both glands. Even granted that the thyroid while in the body has supplied more secretion, it does not follow that it contains more within its substance, since it may have been excreted more rapidly. At present, therefore, it must be agreed with Magnus Levy (49) that the "question of 'dysthyreosis' has not been answered at all satisfactorily from a chemico-physiological viewpoint." All statements made in this direction are purely speculative."



If we accept that there is an increased thyroid secretion in exophthalmic goiter, and such an assumption has much probability, there remains quite a number of symptoms such as exophthalmus and Grafe's sign which cannot be explained as "functions" of the thyroid gland (50).

To sum up: from all these statements, it can be concluded that in the disease complex of exophthalmic goiter the thyroid gland plays an important part. Indeed it can be said that it is always enlarged. But it is not the only organ whose altered function determines the symptoms. Other organ systems such as the nervous system, and the endocrine glands are involved, and disease of the thyroid itself may depend on a primary disease of the central nervous system.

The question of the way in which *the nervous system is involved* has not been cleared up, but certain starting points can be found in the mass of observations which we will presently discuss. The oldest theories considered exophthalmic goiter an actual nervous disease, believing that a change in the sympathetic nerve occurred first, through pressure by the goiter. But the symptoms cannot be fully explained as either pure paralysis, or as pure overstimulation, or by a combination of stimulation and inhibition, although Claude Bernard did succeed in producing exophthalmus in animals by stimulation of the sympathetic nerve. The same is true of the vagus nerve. Certainly in some of the symptoms such as vascular distention, the sympathetic must be involved; and in others, such as tachycardia, the vagus. But this does not justify the assumption that a lesion of these nerves is the principal factor in the disease complex. With its fluctuating, often unequally developed symptoms, exophthalmic goiter appears to be anything else but a circumscribed organic nervous lesion, quite apart from the fact that anatomical changes have never been discovered in nerve areas. Recently, quite a large number of authors distinguish a vagotonic and a sympathetotonic exophthalmic goiter (51). The first shows less tachycardia with less exophthalmus, but subjectively, considerable cardiac disturbance, diarrhea, and sweating. In the sympathetotonic type, marked tachycardia and exophthalmus are present with minor subjective cardiac trouble, but no diarrhea and sweating. But this division unquestionably does not do justice to the clinical picture. It must be said with Hildebrand (52) "that the types named are rarely seen in pure form, and that generally the symptoms are mixed." The same objections may be brought against the investigations which aim to interpret exophthalmic goiter as an organic disease of the central nervous system (lit. Sattler (40)). Occasionally, it is possible to elicit such isolated Basedow symptoms as exophthalmus (53), tachycardia and similar signs, by injury of the medulla oblongata, but the typical disease has not been created. On the other hand, actual focal diseases of the medulla

develop quite different clinical symptoms. On the whole, neurology has practically abandoned the theory that it is a nervous disease of organic origin, with a circumscribed special location, but rather believes that there is a certain general inferiority of the nervous system. Neuroses, constitutional weakness, predisposition, are the terms with which these viewpoints, essentially similar, although differing in details, are characterized. With this assumption in mind it is then conceivable that this inferior nervous system is especially sensitive to excess thyroid secretion. It is true that in the acute variety ("war-Basedow's" (54)), which occasionally results from excitement or terror in individuals with previously healthy nervous systems, it is tempting to think of central stimulation of the secretory nerves of the thyroid, somewhat in the manner as the experiments of Asher and Flack have shown.

The theory, that *other endocrine glands* are also diseased, seemed to be more reasonable from experimental grounds. First the adrenals were suspected because part of the so-called Basedow phenomena such as tachycardia, exophthalmus, glycosuria a.o. are "adrenalin" symptoms (11). They point to stimulation of sympathetic fibres, and it was believed for some time, that an increase of adrenalin could be demonstrated in the blood (45), (55). But O. Connor (56) has shown that technical errors were made. Gottlieb (11) and Frohlich on the basis of these different considerations, came to the conclusion that because of increased thyroid secretion, the organs supplied by the sympathetics become especially sensitive to adrenalin. A similar action is known of cocain. According to investigations of Kepinow (see Gottlieb), the hypophysis may also be involved in this sensitization of the sympathetic system. Furthermore, the experiments of Capelle and Bayer (57) have shown that adrenalin is not well tolerated by patients with Basedow's disease. In those obscure cases of sudden death after operation for exophthalmic goiter (52) such adrenalin action may be suspected. In local anesthesia, patients almost always receive adrenalin, the action of which is increased if combined with cocain, as stated above. It is still an open question whether the number of deaths following operation is diminished if general anesthesia is used. Frank (58) showed that the tremors of exophthalmic goiter are probably similar to those seen normally after adrenalin injections. He speaks of a "sympatheticogenic" tremor (see also "extremities"). But when all is said, this excessive adrenalin secretion theory cannot be reconciled very well with the observation of actual cases of combination of Basedow's and Addison's diseases in which the adrenals were absolutely destroyed by tuberculosis or atrophy (59).

In a recent work of Hofstadter (60) our knowledge of the *part played by the hypophysis*, is collected. Three especial symptoms of this disease

are possibly related to the hypophysis, *viz.*, polyuria, instability of body temperature, and the occasionally observed increased growth in height (61). But in this point also attempts are made at an explanation of only single symptoms and that on the basis of our other knowledge of the hypophysis and not with the direct proof that this gland secretes less or more than normal.

Pettavel (62) describes a case of Basedow's disease in which the patient had shown glycosuria, and changes in the islands of Langerhans could be demonstrated at autopsy.

### THE THYMUS GLAND

The thymus, of all internal secretory glands, has gained much more practical importance in the exophthalmic goiter problem than the adrenals or hypophysis, since Garre (63) reported his case in which thyroidectomy produced no result, and cure was only effected by removal of an hyperplastic thymus. On the basis of Garre's information, other surgeons have removed the thymus in Basedow's disease, and a number have reported cases in which, similar to Garre's case, thymus removal alone brought about a cure or considerable improvement (64). But before we discuss this relation of the thymus more fully, we must consider what we know of the functions of this gland.

Hammar's (65) work tells of *its morphology and development*. From the anatomical standpoint, the fact that the thymus cannot be compared to a lymph node, on account of its epithelial ground substance, justifies the assumption that it is a secretory organ. Our knowledge of its physiological importance is based chiefly on extirpation experiments of which many have been done. (Full compilation and a critical review of the literature can be found in the collective references of Hart, Matti, Klose, Biedl, etc. (10), (66)). These experiments apparently give very irregular results, but this depends as a whole on technical errors, and after his review of the literature, Matti may be justified in concluding, "that of all works which report absolutely negative findings after thymus extirpation in mammalia, not one can withstand expert criticism." Successful experiments depend above all on a complete and early removal, this means in quite young animals, for the function of this gland is exerted chiefly during earliest youth, and it is soon relieved or supported by other endocrine glands. Anatomically, this importance in metabolism, which decreases with advancing age, is shown by its relative greatest weight and measurements in earliest youth. In normal adults there is some tissue, mainly fat, in the place of the thymus. If then, the thymus has been completely removed from a dog or any other mammal during the first weeks of its life, the most remarkable symptom that will be observed is a



decrease of body weight as compared to that of others in the same litter. Certain fluctuations are present. The animals become bloated in appearance, and in the first two to three months, show more fur, so that they appear better nourished than the control animals (adipose stage). But this is misleading, because the total weight of the operated animal is always less than that of the controls. In spite of a good appetite, this difference becomes more and more marked during the following months. Soon it is noticed that the thymectomized animals, which have a rough coat, show retardation of growth, and this developmental check seems to affect the legs especially. They remain short, and the bones become crooked, with swollen, turgid epiphyses; the other skeletal bones also show arrested growth; the body remains small, and the skull appears broad and clumsy. If the bones are examined at this stage, they are found to be softer than those of a normal animal of similar age; and microscopically they show a picture similar to that of rickets. In fact, in all their details, the disturbances of endochondral ossification, the macroscopical swelling of the epiphyses of the bones of the legs, and the rosary, resemble rickets very markedly. These changes affect all the bones and in all parts of the skeleton lime free (osteoid) bone tissue can be demonstrated.

The actual habitus of these thymectomized animals, in addition to the position forced by these "rachitic" bone changes, depends on a peculiar muscular atrophy or muscle degeneration which is especially pronounced in the muscles of the hind quarters. This makes the gait more insecure than if it were due only to the bone changes. In later stages, this muscle disease progresses to such an extent that the animals can hardly stand. The general nutrition becomes steadily worse, until death occurs from a most severe cachexia. Thus, it is chiefly a metabolic disturbance especially in regard to the calcium balance, which leads to the arrested development observed in thymectomized animals. In fowl, this disturbance of calcium metabolism is shown in that they often lay eggs with a shell deficient in lime, or without shell at all (66). At autopsy anatomical changes are found in the other endocrines, especially in the thyroid, adrenals and the generative glands.

These findings again show that some correlation exists between the endocrine glands, but at present the relations are very obscure mainly because the findings are not uniform. The relations of the generative glands to the thymus are brought out even better by castration since after this procedure in young animals, normal thymus involution is delayed (see above).

Experiments, to study *the functions of this gland* more in detail, were made by the injection of thymus extract, or its juice, and by implantations (67), (66). The symptoms which appear can, of course, be considered



specific only if they give uniform results. The accidental findings recorded in such cases are practically valueless in respect to thymus function, for they are due to the action of toxins which are found, non-specifically, in many tissues. To these belong the disturbed general state of health, diminished appetite, loss of weight, pulse acceleration, etc. It is interesting that after extirpation of the thymus it is impossible to improve or eliminate the symptoms, by the injection of its juice intravenously or subcutaneously. Quite the contrary, the animals always show such severe toxic symptoms, that Klose and Vogt believe the treatment of thymectomized animals with thymus preparations accentuates the symptoms caused by the loss of the gland. This negative result is of great importance in our conception of the functions of the thymus. Without doubt, conditions are even more complicated than in the other endocrine glands from which it is possible to prepare a more or less pure substance, which, when administered to other animals, deprived of the corresponding glands, replaces either completely or in part, the functions of the particular gland removed. To sum up: it is unknown whether the active substance of the thymus is in a form of pre-stage, or whether it is an especially sensitive ferment or pre-ferment, or finally, whether the function of this gland is perhaps quite different from that which we believe it to be. Investigations of the ferments have led to only very general results.

Since we know so little of its normal function, it is clear that *its function in disease* is still more difficult to understand. This applies especially to its place in the disease complex of exophthalmic goiter (68). In the cases of sudden and unexpected death after thyroidectomy, an enlarged thymus is found not rarely at autopsy (Capelle, Klose). With such findings, it was first thought that the patient was asphyxiated. But since Garre reported the first cure of exophthalmic goiter by extirpation of the thymus, and a number of other authors achieved good results from this procedure, when thyroidectomy alone proved a failure, it was natural to assume that the thymus played a "chemical" part in the disease similar to that of the thyroid itself (thymogenous Basedow's (69)). "The conditions for a future Basedow's disease are laid down in the branchiogenic organs while the inciting mechanism starts in the nervous system." Consequently, Hart differentiates between a thyrogenous, thymogenous and a thymo-thyrogenous exophthalmic goiter. But we must use great circumspection in evaluating the experiments in which investigators injected or implanted into animals thymus gland removed from patients with enlarged thymus or with exophthalmic goiters and who died with apoplectiform convulsions. All that was said above in regard to injection experiments holds good for these; it is always necessary to distinguish between the toxic action inherent in every tissue, from any specific action

which may possibly be present. The experiments of Bircher (67) are doubtless the most interesting, since he obtained a complete picture of Basedow's disease in five dogs by means of Basedow-thymus. The animals, one of which is pictorially reproduced, developed in four days not only exophthalmus with other eye symptoms which disappeared completely only after five months, but also tachycardia, tremors, and what is of exceptional interest, in four weeks they had developed soft goiters which persisted. Undoubtedly, these findings are very remarkable, and do not lose any value because other authors did not obtain similar results with similar experimental procedures.

What these different results, these accidental findings, show is that the question of exophthalmic goiter is not simply a chemico-physiological one which can be disposed of by such terms as "dysthyroidism" or "dys-thymisation," but that the conditions are very complex indeed, and at present, by no means clear. It is most remarkable how the statements of different authors contradict each other in reference to success or failure from thymus extirpation in exophthalmic goiter. The last reports from even Garre's clinic show that the failures from this operative method are many (70). Other surgeons refuse altogether to have faith in this procedure. Indeed Melchior believes that the statement made above that death following exophthalmic goiter operation is due to the thymus, has been disproved for a long time by the facts (71).

According to the reports of v. Haberer, there seems to be a regional difference in the involvement of thyroid and thymus in exophthalmic goiter. The microscopical investigations of Klose have demonstrated certain typical recurring changes in the thymus in *Basedow's disease*. Time will show whether the conception "*Basedow's disease*" can be sustained as a distinctive disease, or whether there is included merely a number of disease symptoms under this name, which, quite analogous to the term icterus, will be separated in time into quite different anatomically separate entities.

Regarding the cardiac disturbances in Basedow's disease and goiter see Krehl's "The Basis of Symptoms." From the viewpoint of the surgeon, it can be stated that the cardiac disturbances considered partly a result of respiratory difficulty, are not relieved by removal of the respiratory impediment (72).

*The thymus gland* is concerned as cause of death not only in cases of exophthalmic goiter, but there are numerous reports of sudden deaths, generally in youthful individuals, who had no exophthalmic goiter, in which, at autopsy, no diseased condition was found except a thymus, remarkably large for the age of the patient (73). To the same group of "thymus deaths" belongs the sudden death in the newborn. In these cases,

it was suspected at first that a mechanical compression of the trachea by the thymus took place. It is true in children that the diameter of the upper thoracic aperture may be too small, and a rather large thymus may obstruct the lumen of the trachea, but it does not always depend on the weight of the thymus but rather in which direction its development takes place, *i.e.*, whether it extends more in length than in breadth (Hotz). Many anatomists are quite skeptical of the possibility that the thymus may mechanically occlude the trachea, since at autopsy, pressure marks are found only rarely on the trachea, and the thymus usually has plenty of space in the anterior mediastinum. Undoubtedly, this question is still in abeyance (74). But from the clinical viewpoint, it must be admitted that in goiter as well, *e.g.*, in the well known small type which dips transiently into the thorax—sudden severe dyspnea and attacks of asphyxia are often observed when astonishingly few findings on the trachea can be found at operation. Swellings of the mucosa, perhaps reflexly elicited, may possibly come into play, at least, it must be taken into consideration.

Patients in whom chronic disturbances from tracheal narrowness are observed often show an occasional disproportion, for some reason, in the space of the anterior mediastinum and in the size of the thymus. These disturbances are difficulty in swallowing, emphysema, and cardiac disturbances (75). If for any reason, a swelling of the thymus occurs, it is thought that a sudden acute obstruction of the trachea with asphyxia develops. In new born infants, such acute swelling of the thymus is observed chiefly from hemorrhage; in older children, it is more probably lymph stasis, or inflammatory changes during infectious diseases or coughing or, what is of special interest to the surgeon, during anesthesia. The compilation made by Klose, who collected 58 such cases up until 1914, shows that such attacks of asphyxia or respiratory difficulty during operation are by no means rare. Without doubt, the number of cases which die without operation, must be much larger.

As stated, the belief that death is due to mechanical factors alone, if the only post-mortem finding is a large thymus, is often received very sceptically, and it prompts the observer to think more of a physiological-chemical element, disturbances in the equilibrium of the endocrine glands, sudden toxemias affecting the heart, etc. Paltauf (76) first pointed this out. According to his opinion there is found in such cases a combination of enlarged thymus, and enlarged lymph nodes, and he believes that a special constitutional anomaly exists (*status thymolymphaticus*) which perverts the function of other organs, especially that of the heart. Thus the death in individuals with *status thymolymphaticus* would have to be considered a heart death, and not asphyxia (77). This doctrine has its special justification in explaining sudden death in adults, in whom the

space in the upper chest aperture is such that it is improbable that the thymus can produce a mechanical closure of the respiratory channels, even if the gland had not undergone normal involution. Of course, it must be pointed out that Paltauf's teaching of the coexistence of enlarged thymus and enlarged lymph nodes is incorrect (Hart, Matti a.o.); on the contrary this combination is observed very rarely. But it does not invalidate the reasoning in Paltauf's teaching, *i.e.*, that some physiological chemical factor is at fault if an enlarged thymus is found at autopsy. We do not know, however, to what this fault is due.

The investigations of Barbarossa (78), who showed that animals without a thymus, are especially resistant to chloroform, and conversely, that after thymus injections the resistance is lowered, leads to the thought of a flooding of the organism with thymus secretion in such sudden deaths. But on the other hand, other experiments with thymus extirpation and thymus juice injection have shown so few positive results, that the answer to this question must be reserved. Because patients with enlarged thymus often have a hypoplastic chromaffine system, with fatty degeneration, and decrease of the chromaffine cells of the adrenal medulla, other writers assume that there is a sudden failure of adrenalin in such cases. Since Wiesel, Schmorl and Ingier (79) proved that the adrenalin content of the blood is decreased by the anesthetic, it is thought that in people with enlarged thymus, *i.e.*, with a hypoplastic adrenal medulla, the decrease of adrenalin content finally leads to a catastrophe. To avoid this, Delbet (80), who carried out extensive investigations on this point, gives his patients adrenalin subcutaneously, before operation, with supposedly good results. But bearing in mind the statements made on a preceding page regarding adrenalin action in Basedow's disease, this injection must be made with due precautions.

If it is desired to consider these questions on the basis of clinical evidence, it must first be emphasized that the deaths occurring with enlarged thymus or enlarged lymphatic apparatus are not always similar. But no differences that are consistent can be demonstrated in the cases with enlarged thymus as contrasted with those with enlarged lymph-nodes.

The type of death in status thymolymphaticus during anesthesia is sudden, often occurring after a few inhalations of chloroform. It is often observed in excited individuals, corresponding to observations in ordinary life in which people suddenly drop dead after powerful psychic disturbances, excitement, etc. (81). Patients, who die in this manner, suddenly, at the commencement of anesthesia, succumb from heart conditions of the type Hering (82) has described and named as "seconds-heart-death."



In another group of cases, death does not occur immediately after or during anesthesia, but hours, even days, later. I observed such a case in a child after an ordinary uncomplicated operation for hernia. The child, a sturdy, perhaps somewhat fat boy, of about four years, did not recover after the operation which had not lasted very long. He remained in a comatose condition, the pulse was poor from the time of operation, and after increasing coma, death took place within 48 hours. At autopsy, in addition to a marked status thymolymphaticus, with exceptionally large lymph nodes in the abdominal cavity, central necrosis and fatty degeneration of the liver were seen. The clinical picture recalled the Eck's fistula dogs reported by Fischler (83).

The deaths after operation in Basedow's disease may be similarly delayed. It is unusual for patients to die immediately after operation, but most often in the evening following, or on the next day. In this case also the chief symptom is heart failure, the pulse is very rapid and not every beat reaches the periphery; finally there is only fibrillation. The hum over the heart, described by Hering as characteristic of "seconds-heart-death," can occasionally be demonstrated in such individuals when in extremis (84). The high temperature may in part be explained by the restlessness, in part, like all temperature increases after thyroidectomy, as absorption fever, bronchitis, or slight wound infection, but whether they fully explain these high temperatures is, of course, undecided. Adler (85) has discovered interesting relations of the thyroid gland to temperature regulation. There are certain changes in the thyroid in hibernating animals and he obtained a rise in temperature from 7 to 8°C. to 34 to 38° in them by the injection of thyroid extract and an increase of respiratory rate with awakening. According to Boldgreff (86) dogs whose thyroids and parathyroids are removed, lose the faculty of temperature regulation.

Goiters which dip into the chest cavity, swellings, and tumors of the thymus, lead to *compression symptoms in the mediastinum*. The most essential function of the mediastinum is to "keep the track clear" (87) and allow a number of organs, essential to life, *i.e.*, esophagus, trachea, large vessels, nerves, etc. to pass through. But the elasticity of the mediastinum is very slight, and, therefore, severe disturbances in these organs occur very quickly in space restricting processes.

The veins offer the least resistance to pressure, and the blood attempts to flow from the root of the superior vena cava by lateral channels into the inferior vena cava. If the lumen of the azygos vein, situated in the posterior mediastinum, is free, which is often the case for a long time, this channel is used. If it is obstructed the blood flows through the subcutaneous veins which then appear as thick bluish red cords. For unknown

reasons, this distention does not occur in mediastinal tumors, and a uniform edema of the neck and upper chest results with bluish red discoloration of the skin (Stock's collar).

In addition to tumors, air collections in the mediastinum (*mediastinal emphysema*) may lead to such life-endangering conditions. Such a mediastinal emphysema may result from trauma, *e.g.*, gun shot wounds, in whooping cough (88) and in operations, for instance, from incomplete closure of a bronchus after extirpation of a lobe of a lung (89).

Compression of the vagus nerve leads either to tachycardia (inhibition) or to bradycardia (stimulation). Paralysis of the recurrent nerve is a diagnostic sign of practical importance in a space decreasing mediastinal process.

The difficulty in breathing in mediastinal tumors is explained by the obstruction of the trachea or bronchi and is perhaps increased by an edema of the affected portion of the mucous membrane, and by lymph stasis. The effects of this difficulty in breathing on the lungs and the body generally, will be discussed later.

The abundant lymph channels and the large lymph spaces of the mediastinum are probably also involved in the compression, but the free anastomoses prevent excessive stasis. But wide dilatation of the lymph channels becomes dangerous when infection appears, which may arise when a phlegmon in the neck or other neighboring situations spreads to the mediastinum. These are usually fatal, since the septic process is able to spread rapidly and unhindered. In chronic inflammatory processes, extensive connective tissue increase occurs which may clinically simulate tumor formation (90).

The second function of the mediastinum, that of partition between the two halves of the thorax, is from a practical surgical standpoint, of great importance in the operative procedures which disturb the equilibrium of the thoracic organs to the right or left (pneumothorax, thoracoplasty). If the mediastinum becomes too freely movable, mediastinal flutter occurs (91). The structural arrangement varies in different species of animals. The dog's mediastinum is very movable, while that of the rabbit on account of its greater breadth, is more rigid. When pneumothorax is produced in a dog, every inspiration pulls the mediastinum and the heart toward the closed side. During expiration, it bulges sharply toward the pneumothorax.

The lung oscillates to and fro but carries on no respiratory movements. In this way, the gas exchange is completely absent in the lung, even though the pneumothorax has not produced cessation of movement. The animal, therefore, becomes deeply cyanosed and suffocates in a few moments. In rabbits, goats, and other animals, in which the mediastinum is not as

movable as in the dog, it is not pulled completely over and against the breathing lung during each inspiration so that the breathing of these animals is interfered with very little. The rigidity of the human mediastinum lies between that of the dog and rabbit. There are, of course, individual differences which depend on previous inflammatory processes in the adjacent pleura, which may increase the rigidity. In cases of extensive thoracoplasty, this mediastinal flutter can be observed directly in the so-called "paradox respiration" (92). The chest wall, from which the bones have been removed, is pulled in during inspiration and expanded during expiration.

### THE PARATHYROID GLANDS

The *parathyroid glands*, which were discovered by Sandstroem in 1880, are in close anatomical relationship to the thyroid (93). Experiments have shown beyond doubt, that the extirpation of all the parathyroid tissue leads to grave and fatal *tetany* (94) (21). The rat lends itself very favorably to these experiments, because its parathyroids are separate from the thyroid gland and they may be injured or extirpated without disturbing the latter structure. This is important, for up until about 20 years ago, tetany, particularly that occurring after goiter operations, was believed to be due to removal of thyroid tissue. Today it can be stated, not only on the basis of these experimental results, but also from the anatomical investigations of Erdheim who showed by serial sections, that the parathyroids were injured or absent in human tetany, that tetany in every case is a result of the failure of function or the absence of the parathyroids. Obviously, the degree of tetany depends on the relative amount of parathyroid tissue which is destroyed.

After operation, the most severe symptoms are seen in the acute variety, in which the patient a short time after thyroidectomy—perhaps in a few hours—develops strong, convulsive spasms with more or less asphyxia, diaphragmatic spasm, great increase in muscle irritability (Chvostek's phenomenon), greatly accelerated heart action, high temperature, etc. This acute tetany generally ends in death in a few hours, but fortunately such cases are extremely rare, and doubt may arise from the clinical picture that it is a true tetany. The diagnosis is usually made because the symptoms followed an operation for goiter and so it is possible that many of the published cases are something entirely different.

The type more frequently encountered, runs a more chronic course and usually begins several days after operation. The symptoms, in general, are milder; the spasms are not clonic, but tonic; certain muscles are especially involved, so that, e.g., the hand assumes the so-called obstetrical position. These patients usually recover, and for this reason the assump-

tion is made either that not all of the parathyroid tissue had been removed, or that it had been only injured. Another possibility has been discovered by the investigations of Erdheim, who frequently found accessory parathyroids capable of function in the anterior mediastinum, embedded in thymus substance, or along the ascending arch of the aorta. V. Eiselberg (95) describes such a case with a very interesting history. The patient, a woman, had had mild attacks of tetany for years following total extirpation of the thyroid gland. These attacks disappeared after some time. Years later, she developed a tumor behind the upper part of the sternum which v. Eiselberg removed with great difficulty. Severe tetany promptly developed. The tumor proved to be an alveolar carcinoma, but it could not be determined whether its origin was a parathyroid gland or some other structure, and whether in growing it destroyed accessory parathyroid tissue in the anterior mediastinum.

In addition to the spasms, certain *trophic disturbances* have been observed in the more chronic forms which find expression in such changes in the teeth as increased growth in length, increased grinding down, and changes in their position, which in animals may interfere sufficiently to cause starvation. Alterations in bones closely resembling rickets have been described (96); fractures heal more slowly; the callous is exceptionally poor in lime salts. In man, the development of cataract has occasionally been observed.

If the patient recover from the acute symptoms, particularly from the spasms, there remains for a long time or permanently, a "latent tetany." That is, these individuals are predisposed to spasms which may arise from causes which in normal persons would produce no effects. These spasms need not be generalized, but may affect particular muscle groups (laryngospasm, etc.; latent symptoms according to Trousseau, Chvostick, Meinert, and others (97)). Since the same phenomena are observed in animals when only a part of the parathyroid apparatus is removed, this experimental "latent tetany" was regarded with great interest because it seemed that more knowledge could be gained of those diseases in which spontaneous spasms arise (98). Among them are the tetany of pregnancy (Frankl-Hochwart), perhaps eclampsia; the tetany of infectious diseases and toxemias; the so-called gastric tetany, and the tetany in children, *i.e.*, spasmophilia.

That pregnant animals, after partial removal of the parathyroids, develop tetany very readily is shown in the experiments of Adler and Thaler (94). The investigations of Iselin (96) come under this heading. He could show that the offspring of parathyroidectomized pregnant rats are very sensitive to injuries of the parathyroids and that they quickly die with the symptoms of the most acute form of tetany. Haberfeld (99)



could demonstrate changes such as sclerosis, round cell infiltration, cyst formation or atrophy in all four parathyroids in a case of tetany in pregnancy. Meinert (97) among others, describes a human case of tetany in pregnancy. In confirmation of the experimental findings of Iselin, just mentioned, the child of this woman developed spasms and died early.

There are a number of isolated observations of tetany occurring in infectious diseases, such as those of Moller (10), who found miliary tubercles in the parathyroid glands.

Another form which is probably related to poisoning with ergot is the so-called *occupation tetany* which occurs periodically among workers in various trades who have their own small shops (cobbler spasm and so on, Frankl-Hochwart). In Vienna, this is observed particularly in the months from January to March when the Russian rye from the last harvest is being used. After March the toxicity of the ergot seems to become diminished. The possibility, however, that an "endemic poison" such as occurs in cretinism, plays a role cannot be entirely excluded (77). Thus far, it has not been possible to examine this view experimentally.

The *tetany* which is occasionally seen in *peritonitis* probably belongs to the same group as that in infectious diseases, or in toxemias (100). It has been observed, as Bircher points out, only in diffuse peritonitis, as, for example, in perforating appendicitis. Anatomical changes in the parathyroid glands have not been found up until now so that it is always questionable whether there is an injury to the parathyroid glands through the absorption of poisons or bacteria from the peritoneum, or whether there is a reflexly produced hypofunction, or whether, perhaps, it is something entirely different. The similarity of the disease picture, at any rate, points to the conclusion that the parathyroid glands are concerned in some manner.

The same may be said of the tetany in diseases of the stomach associated with obstruction (*tetania gastrica*) (101), (100), but in this case as well, it is only the similarity of symptoms which points to participation by the parathyroid glands, for even if Haberfeld (99) did find anatomical changes in them in one case, there are the negative findings of Erdheim and others in contradiction. Stasis and decomposition of stomach contents are certainly important, but in spite of all efforts, a cramp producing toxin could not be recovered from the contents. When the stasis is relieved by gastroenterostomy, the tetany disappears. An increased viscosity of the blood is said to be important (101). Just what part is played by the desiccation which results from inflammatory changes in the absorptive powers of the intestinal mucosa is not known with certainty, but the theory of desiccation as cause of the tetany has now been aban-

doned (102). A collective cause of stomach diseases and tetany has been ascribed to the vagus nerve.

The tetany of children, which is now usually given the name of spasmophilia or the *spasmophilic diathesis*, cannot be distinguished by clinical symptoms (103) from parathyroid tetany, even if anatomical lesions (hemorrhages, etc.) have been found in only a very few cases (104), (64). The increase of tetany in children in the spring of the year is interesting. According to Moro (105) all internal secretory glands are more active during this season, but this statement does not explain the fact. How much the development of spasms is influenced by inexpert artificial feeding is also unexplained at present, although it is of course easy to build up theories (106). The experiments of Iselin related above, show very prettily how the development of such a tendency to spasms in children may be visualized.

Very little is known of the relations of the parathyroids to true *epilepsy*. The convulsions in the latter disease are entirely different from those in tetany. But new observations, time and again, seem to point to relationships between them, as for example, the changes in the dental enamel in epileptics (Redlich). Experimentally, epileptic attacks in addition to tetany, have been observed after removal of the parathyroids and certain parts of the brain (107). Clinical observations are also recorded in considerable numbers, in which coincident with and after tetany, epilepsy has developed, or in which a childhood spasmophilia was transformed into an epilepsy (lit. see Bauer (77), (108)).

Further, *myotonia* has been brought into relation with the parathyroids (109); myasthenia is regarded as due to a hyperactivity of the parathyroids (110) without, however, it having been possible to demonstrate myasthenic muscle reactions in animals with hyperfunctioning parathyroids (96); chorea minor, paralysis agitans, spatrachitis (108) (Curschmann), osteomalacia and ostitis deformans are other conditions which have been placed in the same category, the last two of which interest the surgeon particularly. But until now, at any rate, the anatomical findings have not been sufficient to justify the assumption of a definite relation between them and the parathyroids (111). But what sort of a causal relationship could there be, especially between the parathyroids and tetany? The latter seems undoubtedly due to a toxemia, which can only be of endogenous origin, *i.e.*, the toxins must be engendered within the organism itself. From this it must be assumed that the toxin, which can best be regarded as an intermediary product of metabolism, is detoxified by intact parathyroid glands. Search for this hypothetical substance has been made by numerous workers and by many methods. Biedl in his critical summary states that nothing certain is known of its composi-

tion, although he himself is inclined to think it is of the nature of amine bases. Under these conditions, it is important for the practitioner only to form an idea of the manner in which the parathyroids are able to bring about a detoxification. Two ways are possible. Either the toxic metabolic products are collected by the parathyroids and through conjugation or other means are rendered harmless (112), or the parathyroids secrete a substance—possibly a ferment—into the blood which detoxifies (113) or protects the organs attacked (nervous system) (108).

The decision as to which is the correct one of these two theories, can be made by examining the results following the therapeutic transplantation and feeding of parathyroid glands (114). There are a large number of such observations on record, which indicate that severe cases of tetany have been improved by such means. Experimentally, it has also been demonstrated that parathyroid transplants grow and function. After a certain time, they are destroyed but it is just this destruction which proves that their function consists in elaborating some sort of a secretion, and not in detoxifying by absorption and conjugation, the hypothetical poisonous metabolic products (115). That the transplantation can be done conveniently under local anesthesia has been demonstrated in the experiments of Passow (116).

The subject, simple though it may seem from what has been said, is not as uncomplicated as it looks. Difficulties of explanation are offered especially by the fact that relief of symptoms of tetany has been brought about by the administration of preparations of the thyroid gland and of iodothyreoglobulin (Kocher). This again emphasizes the close relationship between the parathyroids and the thyroid as well as between other internal secretory glands (117). The latter proposition has been brought out by experiments such as those of Guleke, who extirpated the thyroid and parathyroids in rabbits, with tetany as one of the results. When the adrenals were removed at the same time, no tetany developed, but when the thyroid was left intact, and the parathyroids and adrenals were both removed, tetany again occurred. This, what might be called antagonism demonstrable in the different glands of internal secretion, has been interpreted by Guleke in this way: the adrenals and thyroid stimulate, while the parathyroids inhibit the sympathetic (see also Rudinger (98)). These reciprocal relations between the thyroid and parathyroids are shown further by the hypertrophy of the latter when the former is removed, and *vice versa* (Vassale and others). According to this, the functions of the thyroid and parathyroids would seem to be similar, and not antagonistic. The relation of tetany to the adrenals is further illustrated in an observation of Th. Kocher, who saw tetany with bronzing of the skin after complete removal of the thyroid. In the present modest state of our knowl-

edge on this subject, however, it is probably better to adhere to the facts gained experimentally, than to draw too far-reaching conclusions from them.

Many experiments such as extirpation of peripheral nerves, or of the spinal cord, have been performed to discover the parts of the body which are affected by this hypothetical poison (118). The interpretation of the results varies with the different authors; this much, however, seems certain, that the tetany toxin does not act on the muscles, but on separate parts of the higher nerve centers. The varying pictures in tetany can be best explained by such an hypothesis (108). That the sympathetic system has its own share in the process seems probable from the work of Falta and Kohn (117).

A discussion of the relation of the parathyroids to calcium metabolism—a subject of interest to surgeons because of the bone changes following parathyroidectomy—may be found in Biedl (10).

#### CAROTID GLAND

Experimental investigations of the functional importance of the carotid gland have been stimulated by the occasional occurrence of tumors (119). Their results are not uniform. Schmidt obtained no consistent findings, either by bilateral extirpation, or by implantation, so that, with Marchand, he is of the opinion, that the carotid gland is a rudimentary organ. On the other hand, Betke, who extirpated the carotid gland in cats after bilateral ligation of the common carotid artery, found not only bone changes reminding him of rickets, but changes in the marrow and in the spleen. What changes were present in the thyroid, parathyroids and adrenals was not decided at the time of publishing this work. But possibly the bone changes mentioned depend on injuries to these organs.

#### THE HEART

The surgery of the heart is essentially the surgery of injuries. The widely accepted belief among the laity that an injury, such as a stab wound, is instantly fatal has been recognized as incorrect for a long time. Hyrtl has described, to mention an example, how a stag shot through the heart, swam across a large body of water. George Fischer published the first larger statistical work on this question, and showed that death occurred instantly in only 26 per cent. of the cases of heart injury, while perfect healing occurred in about 11 per cent. of the cases (122). Among these latter, a needle or a thorn were the instruments in seven instances; in five cases, a bullet remained lodged in the heart for years without giving rise to any trouble.



It had been shown in the early nineteenth century by Bretonneau, Larrey, and others (123) that piercing the heart of an animal with a needle produced no recognizable disturbance. According to the experiments of Kronecker and Schmey (124) it is only when the injury involves a certain region, *viz.*, the bundle of Hiss, that sudden death occurs. How far this applies to man is not established as yet, but cases occur in which a lightning like death occurs in man after punctures (G. Fischer).

The cause of death in cardiac injuries is quite involved. If there is no large wound to the exterior, the question of hemorrhage does not enter, because the heart is embarrassed and hindered in its movements by the blood poured into the pericardium long before the loss of blood makes itself felt. This is called "heart tamponade," a pathological process known already to Morgagni (125). Experimental study of the effects of such an effusion into the pericardium has been made by many investigators. After injecting oil into the exposed pericardial sac of dogs, the arterial pressure falls, and the venous pressure rises in proportion to the rise of pressure in the sac (126). According to Molitoris (127) the pathological processes are quite complicated even though they seem simple enough. Following slight injury, the blood pressure falls because of the pulling action of the blood in the pericardium and the increased pressure against the cardiac walls. At first, the fall in blood pressure is purely reflex, and is brought about by dilatation of peripheral vessels. The vagus is stimulated, and the heart rate becomes slower with the result that the outflow of blood from the wound in the heart is diminished and filling of the pericardium is slowed. Moreover, the rate of outflow of blood from the opening in the heart is influenced also by changes in the degree of expansion of the lungs, according to Sauerbruch (128), but this idea is not quite correct as has already been detailed. Can there not be a vagus irritation in this connection?

That a wound in an animal's heart can be closed by suture was shown quite early by Del Vecchio (cited by Barth). Many others have repeated these experiments and demonstrated that cardiac action is not disturbed by such a procedure (129). As is known, Rehn (130) was the first to successfully suture the heart in man.

Injuries to the coronary arteries lead to heart tamponade just as wounds of the heart itself. The demonstration that they are not end arteries as Cohnheim believed, is very important in the question of their ligation. But even if anastomoses between the two coronary arteries have been demonstrated by Hirsch, Spalteholtz and many others, the sudden ligation of one or the other is certainly not an entirely safe procedure.

The numerous experiments have shown that ligation is borne differ-

ently by different animals; that certain points of ligation are more dangerous than others, and that in thrombotic occlusion of the coronaries, a great difference in results occurs if the occlusion is gradual or rapid (131). Unfortunately, a surgeon will not be able to practice the teachings of these experiments, but will be compelled to transfix and ligate the bleeding point under all circumstances.

In serous pericarditis—one of the few affections of the heart which occasionally needs surgical interference—the danger of heart tamponade is not particularly great, in spite of large effusions because the fluid collects slowly and the pericardium can adapt itself to it. If paracentesis fails in such cases, a window may be cut in the pericardium, as Laewen (132) and others have described, to allow egress into the pleural cavity.

Dry pericarditis is also occasionally adapted to operative interference, as was pointed out principally by Brauer (133). Among pericardial adhesions, the so-called massive internal ones between parietal and visceral pericardium often lead to complete obliteration of the pericardial sac. These require no operative procedures. But when the inflammatory process extends to the neighborhood and involves mediastinum, lungs, diaphragm, and sternum, so as to produce adhesions to the heart, it is often necessary to restore movability to these structures in order that the heart, which can scarcely beat, may be better able to contract (*e.g.*, by extensively removing the ribs).

The experiments of Goringstein (134) detail the manner and the paths by which foreign particles such as bacteria or dyes are absorbed from the pericardium.

Blunt force may also produce varied wounds and injuries as can be determined from the experiments of Fischer (122), Schuster, Heidenhain (135) and others. Autopsy investigations of this subject have been made by Barie (136). The facts are of occasional interest in the judgment of certain accident cases. Such trauma is also felt by the heart when attempts are made by massage, to bring the standing heart into activity. The anatomical changes found in this connection have been described by Bohm (137). There are more or less fine or coarse injuries to the muscle fibres.

Leporski (138) has investigated the effects of light pressure and slight injury to the surface of the heart. He found that even a slight injury was followed by a fall in the blood pressure and later by fibrillation.

#### LITERATURE TO THYROID

1. Kocher: Arch. fr. klin. Chir., 1883, V. 29, p. 254.
2. Vincent: Thyroid function summary, *Ergebn. d. Physiol.*, 1911, V. 11.
3. Horsley: *Festschrift. f. Virchow*, Berlin, 1891; August Hirschwald, V. 1, p. 369.

4. Luthi: Mitteil. a. d. Grenzgebieten, V. 15.
5. Baumann: Zeitschft. f. physiol. Chemie, 1896, V. 21 u. 22.
6. Oswald: Die Schilddrüse Leipzig, 1916, (Veit and Co.) (lit.).
7. Gottlieb: Deutsche med. Wochenschrift., 1896, p. 235.
8. Kendall, E. C.: Collected papers of the Mayo Clinic, 1915, 7, 393; 1916, 8, 513; J. Biol. Chem., 1919, 39, 125.
9. Notkin: Wiener med. Wochenschrift, 1896; Blum: Berlin. klin. Wochenschrift., 1898.
10. cit. by Biedl: Innere. Sekretion 2 edit., 1913, Urban and Schwarzenberg.
11. Gottlieb: Deutsche med. Wochenschrift., 1911, p. 2161.
12. Reid Hunt: J. A. M. A. 1907.
13. Trendelenburg: Biochem. Zeitschrift., 1910, 29.
14. Quervain: Mitteil. a.d. Grenzgebieten, Suppl., Vol. 1904.
15. Asher and Flack: Zentralbl. f. Physiol., 1910, V. 24 u. Ziegl. Beitrage, 1910, 55.
16. Andreson: Arch. f. Anat. u. Entwicklungs-, 1894. Sarbach: Mitteil. a.d. Grenzgebieten, V. 15.
17. Eppinger: Zur Pathologie u. Therapie d. menschl. Odems, Springers Verlag., 1917.
18. v. Bergmann: Zeitschrift. f. experim. Pathol., 1909, V. 5.
19. Rogowitsch: Zieglers Beitrage, 1889, V. 4.
20. Zietzschmann: Mitteil. a.d. Grenzgebieten, V. 19, p. 353. Lanz: Volkmanns Sammlung klin. Vortr., 1894. Rogowitsch: Arch. f. Physiol., 1888. Hofmeister: Bruns Beitrage, 1894, V. 11. v. Eiselsberg: Arch. f. klin. Chir., 1895, V. 49.
21. Hagenbach: Mitt. a.d. Grenzgebieten, 1907, V. 18.
22. Falta: Handbuch d. inneren Medicin, 1912, V. 4, p. 445. Kottmann: Zeitschrift. f. klin. Med., 1910.
23. Hanau: Arch. f. klin. Chir., V. 60, p. 247. Steinlein: Arch. f. klin. Chir., 1896, 60. Bayon: Verh. d. physik.-med. Ges. Wurzburg, 34-35.
24. F. K. Walther: Deutsche Zeitschrift. f. Nervenheilkunde, 1909, 38. Marinesco and Minea: Compt. rend. Soc. Biol., 1910, 68.
25. Eppinger: Mitteil. a. d. Grenzgebieten, 1918, Festschrift. f. v. Eiselsberg.
26. Rudinger: Zeitschrift. f. klin. Med., 1908, 66.
27. Magnus-Levy: Berliner. klin. Wochenschrift, 1903 u. Zeitschrift. f. klin. Med., 1904, V. 52. v. Eiselsberg: Naturforschervers, 1913; Wiener med. Wochenschrift, 1902. Kocher: Deutsche Zeitschrift. f. Chir., 1892, V. 34. Bircher: (myxedema) Deutsche Zeitschrift. f. Chir., V. 98. Kutschera: Wiener klin. Wochenschrift, 1909-1910, p. 771. Christiani and Kummer: Munchener med. Wochenschrift, 1906, p. 2377.
28. Enderlen: Mitteil. a.d. Grenzgebieten, 1898, V. 3.
29. Klose: Ergebn. d. Chir., 1914, V. 8, p. 274.
30. Summary cf. Bircher: Ergebn. d. Chir., 1913, V. 5 u. Ergebn. d. Patholog., 1911, V. 13. Kutschera: Wien. klin. Wochenschrift., 1909 u. 1910. Biedl: l.c. Dieterle, Jahrb. f. Kinderheilkunde, V. 64, p. 576. H. Bircher: v. Volkmanns Sammlung klin. Vort., 1890, No. 357. E. Bircher: Brun's Beitrage, V. 89, p. 1. v. Eiselsberg: Die Chirurgie d. Schilddrüse in Deutsche Chirurgie, 38, V. 1. Ewald: in Nothnagels Handbuch, 1909. Hart: Berliner. klin. Wochenschrift, 1917. Schlagenhauser u. Wagner: v. Jauregg. Beitrage zur etiologie u. Pathologie d. endemischen. Kretinismus, Leipzig u. Wien., 1910. Isenschmid: Med. Klink., 1917. Hirsch: Handbuch f.d. hist.-geographischen Pathologie, Stuttgart, 1883.

31. Breitner: Mitt. a.d. Grenzgebieten, 1912, V. 24 u. Wiener klin. Wochenschrift, 1912. Blauel and Reich: Bruns Beitrage, V. 83. Schlagenhauer and Wagner: v. Jauregg Beitrage z. Aetiologie u. Pathol. d. endem. Kretinismus Leipzig and Wien, 1910. Wilms: Zentralbl. f. Chir., 1910 u. Deutsche med. Wochenschrift., 1910. Bircher: Deutsche Zeitschft. f. Chir., 1910, V. 103; Zeitschft. f. exp. Path. and Ther., 1911; Med. Klinik., 1910; Zeitschr. f. Chir., V. 112. Hirschfeld and Klinger: Munchener med. Wochenschrift, 13.
32. H. Bircher: Der endemische Kropf. usw. Basel, 1883.
33. Kocher: Vorkommen u. Verbreitung d. Kropfes inn. Kanton Bern., 1889.
34. Lobenhofer: Mitteil. a.d. Grenzgebieten, 1912, V. 24.
35. Hesse: Arch. f. klin. Med., 1911, V. 102, p. 217.
36. Schittenhelm and Weichardt: Der endemische Kropf. Berlin., 1912.
37. Dieterle, Hirschfeld and Klinger: Arch. f. Hyg., 1913, V. 81, p. 128.
38. Mansfeld and Fr. Muller: Pflugers Arch., V. 143, p. 157.
39. Reich and Blauel: Bruns Beitrage, V. 82.
40. Summary c.f. Lattler: in Graefe-Samischs Handbuch d. Augenheilkunde, 1909, 4. Mobius: in Nothnagels Handbuch, 1896, 22. Chvostek: in Enzyklopadie d. klin. Med. Julius Springer, 1917. Enlenburg: in Ziemssens Handbuch, 1875, V. 12. Fr. Kraus: in Ebsteins Handbuch, 1899, V. 2. Magnus-Levy: in v. Noordens Handbuch, 1907, V. 2. Melchior: Ergebn. d. Chir., 1910, V. 1.
41. Wendelstadt: Deutsche med. Wochenschrift, 1894. Lanz: Mittheil. a. d. Grenzgebieten, 1901, V. 8 u. Deutsche med. Wochenschrift, 1895. Buschan: Deutsche med. Wochenschrift, 1895. Furth: Ergebn. d. Physiol., 1909, V. 8 (lit.).
42. v. Salis and Vogel: Mitteil. a.d. Grenzgebieten, V. 27, p. 275.
43. Kocher: Arch. f. klin. Chir., 1910, V. 92.
44. Marine, D., Kimball, O. P. and Rogoff, J. M.: "Prevention of simple goiter in man," J. Lab. and Clin. Med., 1917, 3, 40; Arch. Int. Med., 1918, 22, 41; Arch. Int. Med., 1920, 25, 661; J. A. M. A., 1919, 73, 1873.
45. Kraus and Friedenthal: Berlin. Klin. Wochenschrift, 1908, p. 1709.
46. Passler: Mitt. a.d. Grenzgebieten, 1905, V. 14. Klose: Arch. f. Klin. Chir., V. 93, p. 649 u. Beitr. z. klin. Chir., 1912, V. 77, p. 601. Pfeiffer: Munchener med. Wochenschrift., 1907, p. 1173. Schonborn: Arch. f. exp. Pathol. u. Pharmk., 1909, V. 60. Schulze: Mitt. a.d. Grenzgebieten, 1907, V. 17. Gley: Journ. de physiol. et. de pathol. gen., 1911, p. 955.
47. Baruch: Zentralbl. f. Chir., 1911 u. 1912.
48. Walther and Hosemann: Zeitschrift. f. d. ges. Neurologie, 1914, V. 23, p. 98.
49. Magnus Levy: Handbuch d. Path. d. Stoffwechsels (herausg. v. Noorden), V. 2, p. 1902.
50. Fr. Kraus: Handbuch d. prakt. med. von W. Ebstein, 1899, V. 2, Morbus Basedow.
51. Eppinger and Hess: Die Vagotonie in V. Noordens Sammlung klin. Abhandl., Berlin, 1910.
52. Hildebrand: Arch. f. klin. Chir., 1918, 111, p. 1.
53. Filehne: Sitzungsbericht d. physik. med. Societat in Erlangen, 1877.
54. Klose: Med. Klin., 1918, p. 1199.
55. Fraenkel: Arch. f. exper. Pathol. and Pharmak., 1909, V. 60.
56. O. Connor: Munchener Med. Wochenschrift, 1911.
57. Capulle and Bayer: Bruns Beitrage d. klin. Chir., V. 72, u. 86.
58. Frank: Berlin. klin. Wochenschrift., 1919, p. 1090.
59. Roessle: Verhandl. d. Deutsch. Path., Ges., 1914.
60. Hofstadter: Mitteil. a.d. Grenzgebieten, 1918, 31, p. 102.



61. Holmgren: Nord. med. Arch., 1909, u. 1910.
62. Pettavel: Deutsche Zeitschrift. f. Chir., 1912, V. 116.
63. Garre: Chirurgenkongress, 1911.
64. Sauerbruch: cited by Hart. Med. Klinik., 1915, 1. Rehn: Arch. f. Klin. Chir., 1906, V. 80. Capelle: Bruns Beitr., 1908, V. 58 u. 1911, V. 72; Munch. med. Wochenschrift, 1908, 2. v. Haberer: Arch. f. Klin. Chir., V. 109; Mitteil. a.d. Grenzgebieten, Volume 27. Klose: Neue deutsche Chir., 1912, 3 and Ergebn. d. Chir., 1914, V. 8.
65. Hammar: Ergebn. d. Anat. u. Entwicklungsgeschichte, 1909, V. 19.
66. Hart: Zentralbl. f.d. Grenzgebiete, 1909, V. 12. Ramzi and Tandler: Wiener. klin. Wochenschrift, 1909. Klose and Vogt: Arch. f. Klin. Chir., 1910, V. 92 and Brun's Beitr., 1910, V. 79. Nordmann: Berliner klin. Wochenschrift., 1910. U. Soli: cit. by Matti. Matti: Mitteil. a.d. Grenzgebieten, 1912, V. 24. Matti: Ergebn. d. inneren. Med., 1913, V. 10. Basch: Jahrbuch f. Kinderheilkunde, 1906, V. 64 u. 1908, V. 68.
67. Capelle and Bayer: Bruns Beitrage, 1911, V. 72. Popper: Akad. d. Wissenschaften, Wien, 1905, 114. Svehla: Arch. f. exp. Path. u. Pharm., 1900, V. 43. Gebele: Bruns Beitrage, 1911, V. 76. Bircher: Zentralbl. f. Chir., 1912, No. 5.
68. Morbus Basedow: collected ref. Glaserfeld. Mitteil. a. d. Grenzgebieten, V. 28.
69. Hart: Arch. f. Klin. Chir., V. 104, p. 347 u. Virch. Arch., 1913, Vol. 214, Med. Klinik., 1915.
70. Naegeli: Bruns Beitrage, V. 115.
71. Melchior: Zentralbl. f.d. Grenzgebiete, 1912, Berliner klin. Wochenschrift, 1917 u. 1919.
72. Blauel, Muller and Schlager: Bruns Beitrage, 1909, V. 62.
73. Wiesel: Ergebn. d. Pathologie, 1911, 2 part. Lit. see Friedjung: in Pfaunders Schlossmanns Handbuch d. Kinderheilkunde, V. 3, 2 edit., 1910.
74. Nissen: Brun's Beitrage, V. 91, p. 694.
75. Deneke: Deutsche Zeitschrift. f. Chir., 1909, 98. Ritter: Bruns Beitrage, V. 91, p. 689. Zesas: Deutsche Zeitschrift. f. Chir., V. 105 (lit.). Cohn: Munchener med. Wochenschrift, 1900 u. Deutsche Wochenschrift, 1901. Lange: Naturforscherversammlung, 1902.
76. Paltauf: Wiener klin. Wochenschrift., 1889, 2; u. 1890, 3.
77. Cf. also Bauer: Konstitutionelle Disposition zu inneren Krankheiten-Springers Verlag, 1917, also Wiesel im Handbuch der Neurologie, V. 4.
78. Barbarossa: cit. by Matti, 66.
79. Schmorl and Ingier: Deutsch. Arch. f. Klin. Med., 1911, V. 104. Wiesel: Handbuch d. Neurologie, V. 4.
80. Delbet: Rev. de chir., 1912, V. 32.
81. Walz: Wurttenb. Korrespondenzbl., 1903, V. 15.
82. Hering: Der Sekunden herz Tod. Springers Verlag, 1917.
83. Fischler: Physiologie der Leber. Springers Verlag, 1916.
84. Rost: Ueber agonale Blutgerinnung Zentralbl. f. Path., 1913, V. 24.
85. Adler: Munchener med. Wochenschrift, 1919, p. 1039 and Pflugers Arch., 1916.
86. Boldgreff: cited in Chirurgen kongress-Zentralbl. 4, p. 435.
87. v. Bergmann: Handbuch d. inneren. Med., 1914, V. 2, Springers Verlag., Die Erkrankung d. Mediastinum.
88. Fr. Muller: Berliner klin. Wochenschrift, 1881.
89. Friedrich: Chirurgenkongress, 1907 u. 1908.
90. Krall: Naturhist. med. Verein. Sekt. Heidelberg, 1913, Munchener. med. Wochenschrift, 1913.

91. Bruns: Beitrage z. Klinik. d. Tuberculose, V. 12.
92. Sauerbruch-Elving: Die extrapleurale Thorakoplastik in *Ergeb. d. inner. Med.*, 1913, V. 10.
93. Summary. Wirth: *Zentralbl. f.d. Grenzgebiete*, 1910, V. 13. Biedl: *Innere Sekretion*; Falta *Die Erkrankung der Blutdrusen* Springer, 1913. Phelps: "Tetanie," in *Levandowskys Handbuch d. Neurologie*, 1913, V. 4. Rudinger: *Ergeb. d. inn. Med.*, 1909, V. 2. v. Frankl: *Hochwart in Nothnagels Handbuch*, 2, V. 11. Laudois: *Die Epithelkorperchen in Ergebn. d. Chir.*, 1910, V. 1. Guelke: *die Epithelkorperchen. Neue deutsche Chir.*, Lief., 9. Mc Callum *Ergeb. d. inneren Med.*, 1913, V. 11.
94. Vassale and Generali: *Arch. ital. de Biol.*, 1896-1906, V. 25, 26, 33. Rouxeau: *Compt. rend. Soc. de Biol.*, 1895, 1896, 1897. Erdheim: *Wiener klin. Wochenschrift.*, 1906, u. *Frankfurter Zeitschrift. f. Path.*, 1911, V. 7. Gley: *Arch. de Physiol.*, 1897 u. 5 *Physiologenkongress Turin*, 1901.
95. Eiselsberg: *Wiener klin. Wochenschrift*, 1906 discussion of Erdheim's paper.
96. Iselin: *Zentralbl. f. Chir.*, 1908 u. *Neurolog Zentralbl.*, 1911.
97. Meinert: *Deutsche Zeitschrift. f. Chir.*, 1908, V. 93.
98. Vassale: *Arch. ital. de Biol.*, 1897, V. 30. Rudinger: *Ergeb. d. inn. Med.*, 1909, 2.
99. Haberfeld: *Virch. Arch.*, 1911, V. 203.
100. Holterhof: *Deutsche med. Wochenschrft.*, 1913. Wirth: *Zentralbl. f.d. Grenzgebiete*, V. 13. Bircher: *Zentralbl. f. Chir.*, 1913.
101. Wirth: *Zentralbl. f.d. Grenzgebiete*, 1910, V. 13. Kussmal: *Arch. f. klin. Med.*, V. 6. Fleiner: *Deutsche Zeitschrift f. Nervenheilkunde*, 1900, V. 5; *Arch. f. Verdauungskrankheiten*, 1901, V. 5; *Munchener Med. Wochenschrift.*, 1903.
102. Jonas and Rudinger: *Wiener Klin.-therap. Wochenschrft.*, 1904. Falta and Kahn: *Ztschrft. f. klin. Med.*, 1911, 74.
103. Finkelstein: *Lehrbuch d. Sauglingskrankheiten*, Berlin, 1911. Escherich: *Munchener Med. Wochenschrift.*, 1907.
104. Erdheim: *Ztschrft. f. Heilkunde*, 1904, 25. Yanase: *Wiener klin. Wchenschrft.*, 1907.
105. Moro: *Munchener med. Wchenschrft.*, 1919.
106. Wickmann: *Handbuch d. Neurologie heraus. v. Lewandowsky*, 1914, 5.
107. Kreidl: *Wiener klin. Wchenschrft.*, 1909, 869.
108. Gratz: *Neurol. Zentralblatt*, 1913, p. 1366. Peritz: *Ergeb. d. inneren Med.*, 1911, 7. Curschmann: *Deutsche Ztschrft. f. Nervenheilkunde*, 1910, 39.
109. Orzechowski: *Jahrb. f. Psychiatrie*, 1904, V. 29.
110. Chvostek: *Wiener klin. Wochenschrft.*, 1908, p. 37.
111. Erdheim: *Sitzungsbericht der Akademie, Wien, Math. naturw. Klasse*, 1907.
112. Wiener: *Pflugers Arch. f. Physiol.*, 1909, 61.
113. Medwedew: *Ztschrft. f. physiol. Chemie*, 1911, V. 72.
114. Wiebrecht: *Bruns Beitrage*, V. 92. Schneider: *Deutsche Ztschrft. f. Chir.*, V. 54. Krabbel: *Bruns Beitrage*, V. 72. Danielsen: *Bruns Beitrage*, V. 66. Eiselsberg: *Beitrage z. physiol. u. Pathol. Festschrft. f. Hermann*, 1908. Bircher: *Med. Klinik.*, 1910.
115. Eiselsberg: *Wiener klin. Wochenschrft.*, 1892.
116. Passow: *Bruns Beitrage*, V. 104, p. 343.
117. Guleke: *Arch. f. Klin. Chir.*, V. 94. Falta and Kahn: *Ztschrft. f. Klin. Med.*, 1911, V. 74.
118. Lanz: v. *Volkman's Sammlung*, 1894. McCallum: *Zentralblatt f. Pathol.*, 1905, V. 76. Falta and Rudinger: *Verh. d. 26 Kongr. f. inn. Med.*, 1909, *Zentralbl. f. inn. Med.*, 1909, p. 548.

119. Schmidt: Bruns Beitrage, V. 88. J. E. Schmidt, Betke: Bruns Beitrage, 1914, 95.  
Marchand: Festschrft. f. Virchow, 1891, V. 1. Monckeberg: Zieglers Beitrage,  
V. 38. Neuber: Arch. f. klin. Chir., V. 102. Kauffman and Ruppanner:  
Deutsche Ztschrft. f. Chir., V. 80. Paltauf: Zieglers Beitrage, V. 11.

## CHAPTER X

### CHEST CAVITY

The pathological physiology of the thoracic viscera is of constantly increasing importance to the surgeon for two reasons, first, because greater possibilities of operative interference in this cavity are at hand since the introduction of methods to control varying pressures; secondly, because the complications arising from diseases of the thoracic viscera, especially pneumonia, and cardiac weakness, often bring to naught the results of our best planned operative procedures. It can safely be said that since the spectre of post-operative suppuration has been vanquished by the introduction of asepsis, the chief danger to surgical patients arises in the thoracic viscera. To control these complications is a most important task for operative surgery.

The lungs are concerned in *gaseous exchange* (1). Inspired air, rich in oxygen, is changed by the diffusion of gases in the alveoli to an air rich in carbon dioxide. Bohr (2) opposing the purely physical theory of gas exchange, has suggested that the lungs absorb oxygen on the one hand and secrete carbonic acid on the other. But this theory, which has an analogue in the oxygen secretion in the swimming bladder of fishes, has not been accepted as normal for the respiration of warm blooded animals (3). But perhaps "secretion" does play some part when there is oxygen deficiency in the tissues (4).

In the processes of *inspiration and expiration*, forces act on two places; on the lungs, and on the thoracic cage. The lungs themselves have a tendency to collapse and return to the condition as in the newborn, so that if the opposing forces acting on the thorax are removed in the living, as for example in pneumothorax, they collapse completely from the activity of their abundant elastic fibres (5). The force with which this collapse occurs can be appreciated from the pressure which must be applied, by high and low pressure apparatus in pneumothorax, to bring the lungs in contact again with the pleural parietes. According to Sauerbruch (6) and Friedrich (6) it amounts to minus 7 mm. of mercury.

This tendency to assume the position of maximum expiration is the chief force opposing those acting on the thorax. These latter are divided into elastic forces and muscle action. After the chest wall is opened at autopsy, not only do the lungs collapse, but the ribs immediately spring outward (Paul Bert cited by Minkowski), and give the impression that



these elastic forces are important in the enlargement of the thorax (7). But this is unlikely, because the tonus of the respiratory musculature is the deciding factor in the living (Minkowski (11)). It can be seen during operations such as resections of the first rib for tuberculosis (Freund's operation), or in extrapleural thoracoplasty, that the ribs spring apart as soon as they are severed from their attachments to the sternum, which shows that there is this elastic tension in the thorax in the living as well. Nevertheless, in inspiration, the muscle power, *i.e.*, the activity of the various costal elevators and the diaphragm is of greater importance. In man, the latter muscle is the most prominent of all in respiration. The so-called auxiliary inspiratory muscles operate either similarly to the costal elevators, or they increase the longitudinal diameter of the chest (the long muscles of the back). The diaphragm and the costal elevators usually work synergistically, but in some forms of poisoning (chloroform), disturbances in this synchronous action may occasionally occur, so that the diaphragm moves as in expiration while the thorax carries out an inspiratory movement (8). The chest muscles and the diaphragm are also interchangeable in their relative power, thus we find increased diaphragmatic respiration in fractures of the upper ribs, or after operations on the pleural wall, and conversely, in diaphragmatic paralysis as it occurs after operative section (9) or in "crutch" paralysis of the phrenic nerve (10) we find augmented thoracic respiration. Furthermore, a greater thoracic respiration is seen with the diminished diaphragmatic movement in pulmonary emphysema, pleuritis or pneumothorax, as well as in enteroptosis (11).

The expiratory muscles need not be as powerful for two reasons, first, because the extended chest collapses on account of its weight after the muscle pull is released, and secondly, the ribs, extended upward and outward from the preceding inspiration, tend to assume the expiratory position again, principally because of the elasticity of the lungs. As expiratory muscles, the internal intercostals and the diaphragm come into play. The latter is forced toward the chest cavity more because of the intraabdominal pressure than because of active contraction. The extent of its movements depends, therefore, not only on muscular contraction, but on the elasticity of the lungs acting on the upper surface and the pressure of the abdominal organs on its lower surface.

The importance of the abdominal muscles in the respiratory act must not be underestimated, for even though they are used but little in the superficial respiration, with which man usually contents himself, their non-use in bedfast patients because of the pain from a recent abdominal incision, leads to insufficient aeration, and favors hypostatic congestion and post-operative pneumonia.

The transfer of the movements of the thoracic and diaphragmatic musculature to the lungs constitutes quite a remarkable mechanism. It results only because of the difference in pressure at the border of lungs and thoracic wall, which equals "the sum of the stretching values which keep the lungs expanded beyond their elastic equilibrium" (12). In the cadaver this "tension difference" is apparent at once, for when the chest cavity is opened, the lungs collapse, and the thorax springs outward. But in the living, this tension difference is added to by the tissue tonus, *i.e.*, the tonus of the lungs and the thoracic wall. For this reason, it is different at various places in the thorax, and is expressed in the so-called negative pressure of the pleural cavity (Donders), which can be measured by introducing a hollow needle. It must be remembered, however, that a pleural cavity with a negative pressure does not actually exist in life, but on all sides the lung is applied closely to the parietal pleural wall, leaving only a capillary space between (13). Burkhardt (14) points out that the conception of "negative pressure" has caused considerable confusion. "The air flowing into the bronchi forces the lungs against the chest wall, and the chest wall presses against the lungs." This is physically incontrovertible. The real difficulty of the question is to demonstrate what forces sustain the lung in its tension; especially what forces re-distend a lung once collapsed. If we start by considering conditions as they exist in the newborn, we know that before respiration begins, the lungs lie collapsed in the posterior thoracic space, lateral to the spinal column. The negative pressure is absent, a fact of importance in medico-legal questions. The lung distends and becomes air containing with the first strong inspiration. It might be supposed that it would collapse with the next expiration, but the air remains in them. Why? According to Keller (15) the bronchioles collapse where they join the infundibula, and thus prevent the escape of air. But even if this statement is correct, it would explain only a minute part of the distention. At least, it would not explain the condition in adults. According to Hermann (16) the chest grows more rapidly than the thoracic organs, and a space is formed with decreased pressure within, *viz.*, the pleural cavity. The necessary result of this decreased pressure would be distention of the lungs by air flowing inwards through the bronchi until they lie against the thoracic wall, and this notwithstanding the elastic forces present within. But what sustains the tension in the lungs before this difference in growth is developed has not been clearly answered. For the present, the pressure of the atmosphere on the bronchial tree must be held chiefly responsible, but the expiratory pressure is probably great enough under normal conditions to overcome the elasticity of the lungs (see Reineboth (17)). According to others, the capillary adhesion between lungs and chest wall, or more

correctly, between the two surfaces of the pleura, is important also. We shall meet this factor again in discussing the re-expansion of a collapsed lung. Stovesand (18) believes this adhesive force is really not very great, although doubtless present, because when he opened the pleura in rabbits, even most carefully, the lungs collapsed at once. But Rosenbach (19) contradicts this statement, claiming that it is not easy to obtain a rapid and complete pneumothorax in animals by simply opening the pleura. This corresponds to observations on man. These capillary adhesions doubtless form gradually, and not with the first respiratory movement because the air filled lungs of a newborn child may collapse completely (20). Rosenbach (19) believes further that a vital tonus is responsible for this pulmonary tension, Sauerbruch (9) says it probably depends on the vagus. But this question cannot be disposed of by regarding it simply as a result of tissue tonus, and more work is needed.

The respiratory movements aerating the lungs differ according to whether the individual is at rest or in motion. At work, not only are the respiratory movements increased, but the mean position which the lungs occupy is altered, *i.e.*, in the final analysis, the tonus of the respiratory musculature is changed. To obtain a clear perception of these conditions, the residual air, or the air remaining constantly in the lungs is distinguished from the reserve air which can be expelled by the greatest expiratory effort. By the greatest inspiratory effort the complementary air is taken in. The mean capacity lies between these three values and is the difference between inspiration and expiration. It is influenced markedly by various pathological conditions (21).

The *respiratory movements* are *controlled* by the respiratory centre situated in the medulla, which in its turn is stimulated by the carbonic acid content of the blood (see Minkowski (1) and Staehelin). When the vagus is cut, slow deep breathing results; normally, the respiratory center is controlled reflexly by this nerve (22). Each expansion of the lung during inspiration leads to expiration, each passive expiration to inspiration. According to Einthoven (23), the right vagus is of greater importance to respiration than the left, which is of more importance to the heart. But all other centripetal nerves, the facial, trifacial, olfactory, optic, and the sensory peripheral nerves, can participate in this regulation, and for this reason, fright, offensive odors, pain, etc. all affect respiration.

It is far more difficult to understand why respiration should occur at such regular intervals than that the regulation of the respiratory center should occur through nerve tracts. The first factor to be considered is direct stimulation by the carbonic acid content of the venous blood. Rosenthal (1) in 1862, found that a pause in respiration occurred—apnea—after increased ventilation, whether that was accomplished by bellows,



or by a few deep inspirations. This he accounted for by improved oxygenation of the blood from the deep breathing. But since it was shown that apnea also occurs when the same air is blown in over and over and thus increased in its carbon dioxide content, and that animals actually may perish from suffocation in these tests (Verworn), it cannot be the improved oxygenation which produced the apnea in Rosenthal's experimental procedure.

That conditions may occur in which oxygenation is the cause of apnea is shown in the fetus which, of course, does not breathe as long as its blood obtains sufficient oxygen through the placental circulation; and furthermore, this was proved by Fredericq's (24) experiment in which he conducted the blood of a dog, the lungs of which were ventilated to their maximum as in Rosenthal's experiments, through the head of another dog. The second dog also became apneic. According to Hasselbach (25) a.o., it is not the carbon dioxide content, but the hydrogen ion concentration of the blood which regulates the respiratory mechanism in this manner. But it is still an unsettled question whether these stimuli carried by the blood to the brain suffice to account for the rhythmicity of respiration. Sauerbruch (9) is of the opinion that the changing volume of the lungs is a stimulus through the vagus. This is conceivable, but does not explain the rhythmic respiration after vagus section, which, however, Minowski attempts to explain by a metabolic process occurring in the central nerve cell itself—"nutrition stimulus." At any rate this "apnea" and its explanation is of great interest not only to the theorist, but even more so to the surgeon who encounters it often enough during anesthesia.

[American and English physiologists have contributed a large share of the work on respiration. There is no doubt that the process is under the control both of the nervous system and of chemicals in the blood. The two gases, oxygen and carbon dioxide, seemed the logical stimulants, and so careful attention has been paid to their behavior under various conditions, and to separate their effects under standard conditions. If an animal is made to breathe carbon dioxide in increasing amounts, the oxygen concentration being maintained, respirations increase both in rate and amplitude in a very precise way. When the carbon dioxide content of the air has reached 5 or 6 per cent. the rate increases four or five times the normal. Since this increase in rate is proportional also to the concentration of free carbon dioxide in the blood, it seems that the effect is due directly to the action of the gas on the respiratory center and not reflexly from irritation, etc. of the respiratory passages. But increasing the carbon dioxide concentration in the blood also increases its acidity, *i.e.*, the H ion concentration, and it may be this latter factor which produces the effect. Scott alkalinized animals by injecting suitable doses of



sodium bicarbonate intravenously, and then found in spite of a normal or decreased H ion concentration, that the breathing of carbon dioxide was followed by an increase in respiration. These experiments were done on decerebrate cats to avoid the errors induced by anesthetics. Furthermore, when acids other than carbonic acid, as for example, hydrochloric acid, are given intravenously, the same increase in respiration cannot be obtained, for death invariably occurs when a sufficient amount is given to increase the respirations equal to inspiring about 5 per cent. carbon dioxide. Carbon dioxide, therefore, has a specific stimulating effect on the respiratory center in addition to its acid properties. The reason for this specific effect has been given by Jacobs who found it is related to the extraordinary ease with which it penetrates cell membranes and makes its presence felt within. After it has entered the cell, it may be that it acts by changing the H ion concentration; at any rate, it is enabled to exert its acidic powers much more quickly and readily than other acids, because of this penetrating ability.

Considering the effect of oxygen, it is easily demonstrated that a decrease of its percentage in the inspired air will lead to rapid, shallow breathing. Deficiency in the blood may be brought about by two other means, *viz.*, diminishing the amount of available hemoglobin to carry it, as in carbon monoxide poisoning, or diminishing the rate of blood flow through the lungs as occurs in decompensated heart disease. Barcroft has suggested that the terms anoxic, anemic and stagnant, respectively, be used to designate these three forms of anoxemia.

As stated, when an anoxemia is begun, it leads to rapid, shallow breathing, which in its turn prevents adequate ventilation, so that, for example, an anemic anoxemia will have an anoxic anoxemia added to it, and so on in a veritable vicious circle.

Finally, this rapid breathing will "wash out" carbon dioxide until the concentration of this substance in the blood becomes much lowered. This tends to "alkalosis," which is compensated by the excretion of alkali in the urine, the conversion of more ammonia into urea, etc. Hyperpnea from any cause such as voluntarily, pain, or perhaps incomplete anesthesia, will also tend to this alkalosis, the condition being termed "acapnia" by Y. Henderson. When this alkalosis is established, or tends to be, the administration of carbon dioxide by inhalation would seem to be the logical procedure, but its use must be attended with caution (26) (see remarks and references on acid-base regulatory mechanism in section on kidney, page 290).]

Furthermore, respiration has considerable influence on the *blood distribution*. It is generally understood that the negative pressure which occurs during inspiration leads to a sucking of the blood into the large

intrathoracic vessels, including the heart itself, without considering the pulmonary circulation. But from the very nature of the problem it has been possible thus far to bring only indirect proofs of this view. The x-ray observations of Hofbauer (27), as well as the anatomical investigations of Hasse (27), must be classed with these. The net result is, that various authors interpret the influence of respiration on peripheral circulation in quite different ways (28). Ledderhose (29) has discussed in detail the interesting inspiratory oscillations in the superficial veins which are of interest to surgeons, especially in varices. There is a contrast in the filling of the arm and leg veins, which is doubtlessly related to intra-abdominal conditions, *i.e.*, diaphragmatic movements. At any rate, Eppinger and Hoffbauer (30) proved with plethysmographic measurements that the upward movement of the diaphragm decreased the volume of the leg and increased that of the arm. Be that as it may, that respiration has an influence on the circulation in the peripheral veins is undeniable, since it can be observed at any time that the veins in the neck subside with deep inspiration and swell on compression. Minkowski (1) emphasizes that the increasing negative pressure when the heart is entering diastole and is easily distensible, is also important.

Our knowledge of the influence of respiration on the *volume and rate of flow in the pulmonary vessels* is even less definite. It must be stated in advance that Lichtheim (31) could demonstrate no change in the blood pressure when the pulmonary artery to one lung was ligated, a finding verified by Tigerstedt (32) and Gerhardt (32). But the latter succeeded in obtaining considerable increase of pressure in the right ventricle after experimental pulmonary fat embolism. According to this, the assumption entertained for some time, that the capillary network of the lungs was so extensive that resistances within them could hardly be capable of affecting the total lesser circulation—cannot be entirely true. But at the same time, it must be realized that the resistance in the pulmonary capillaries is always exceptionally low, from which it follows that increase of blood pressure in the lesser circulation leads directly to an increase of the blood capacity of the lungs. Therefore, the lungs, in this relation, occupy a special position among the organs, because in a limb, or in any other organ, the result of increase of blood pressure is increased rate of blood flow, without increase in the actual quantity present at any one time (14).

But in addition, the blood content of the lungs depends not only on the blood pressure maintained by the heart, but also on the pressure in the pulmonary blood vessels themselves, and then not only on that within the blood vessels, but also on the pressure in those outside of the lungs. This has been beautifully illustrated in the experiments of Jager (cited by

Burkhardt). He placed lungs removed from the body, into an airtight glass container and regulated the pressures within the trachea, pulmonary vessels, and the space of the container, the latter representing the pleura. This procedure demonstrated that incorrect figures are obtained if the pressure in the pulmonary arteries and veins is not equalized with the pleural pressure. This factor has often been neglected.

In the third place, the blood content of the lungs depends on the pressure within the alveoli.

The values of these different factors necessarily change during inspiration and expiration, in pneumonic processes, in pleural exudates, or in pneumothorax. There is a difference of opinion, not completely reconciled, on whether a collapsed lung contains more blood than one distended with air. Ebert (33) calls attention to the necessity of differentiating between inspiration and expiration and the position in the inspiratory or the expiratory phase. Sackur (34) found less oxygen in the blood in the carotid arteries after complete collapse of a lung, from which he concluded that the collapsed lung in pneumothorax took up practically all of the blood in the lesser circulation, and it could not be oxygenated. Therefore, the animal asphyxiated. Sauerbruch (6) supported this idea, which has been given the name of "short circuit theory." Unfortunately it has been proved incorrect. Brauer (35) very tellingly says the blood content is not proportional to the degree of distension of the lung, but to the pressure difference between pleura and bronchial tree. It is self evident in pneumothorax, that this difference is always less than normal, and the result must be greater compression of the capillaries with a diminished amount of blood in the collapsed lung. Even the experiments of Cloetta (36) and Rohde (14) cannot alter this logic. As Burkhardt (14) points out, the pressure changes did not involve the large vessels in these experiments; therefore, the results, interesting though they are in detail, cannot be applied to pneumothorax (see previous page) and Bruns (37) showed in his experiments, that the blood content of the collapsed lung is demonstrably decreased after even a few seconds. Propping (38) reinvestigated this work and proved its correctness. Lohmann and Muller (39) arrived at similar results; by one experimental procedure they found no difference in the blood content of the collapsed and the aerated lung, while in another the blood content of the aerated lung was increased as compared to that of the collapsed lung. Gerhardt (32) investigated the effect of artificial exudates, and found that when small in amount, they did not impede the capillary circulation; it was only after exudates large enough to produce respiratory disturbances were formed, that resistance in the capillaries from increase of pressure in the lesser circulation was obtained.

During inspiration and expiration the conditions in the pulmonary circulation are exceedingly complex. Tendeloo (12) constructed a model of tubes intended to represent these blood vascular conditions. He concluded that the vessels are longer and less tortuous when the lungs are slightly expanded and this increases their capacity. With further distention the vessels flatten out, which possibly lessens their total capacity. But in the complicated circulation in the pleural cavity, it would lead to wrong conclusions, if excess value were placed on any one factor, in this case, the capillary network of the lungs. Ebert (33) in his investigations, has avoided this one-sided viewpoint, and found that the pulmonary circulation is improved during inspiration, and impeded during expiration. Neither the air content of the lungs *per se*, nor the density or rarity of the air inspired, has an appreciable influence on the pulmonary circulation. These experimental results correspond very well with the prevailing opinion supported by Bohr, that the lungs are supplied with more blood during inspiration than during expiration.

Regarding the changes in the circulation of the chest by increase in the intraalveolar pressure, *i.e.*, with the third factor mentioned above, it was shown and can easily be recognized by anyone, that during coughing, or any act increasing abdominal pressure, as defecation, a swelling of the neck region occurs. This denotes an impeded venous return flow. Gerhardt and his pupil Romanoff (40) demonstrated in animals, that an increase of pressure of even 8 mm. mercury in the bronchial tree leads to such a severe impediment of the pulmonary circulation that not merely is the pressure in the pulmonary artery and in the jugular vein increased, but the pressure in the carotid artery falls. Pathological processes in which expiratory dyspnea occurs, as in chronic coughs, lead, therefore, to manifestations of congestion in the right ventricle (hypertrophy and dilatation (6), (41)).

If the chest wall is suddenly opened without taking due precautions, the patient may collapse rapidly with urgent dyspnea. This may be designated as "*pleura-reflex*." Many workers have recently experimented exhaustively with this question (42). Accordingly, a large number of cases described as "*pleural reflexes*" may be considered as suffering from arterial air emboli (Brauer, see later). On the other hand, there is a possibility that reflexes can be incited from the pleura which possesses abundant modified Paccini bodies (43), but this reflex depends not only on the sensitivity of the pleural cavity, but also on that of the different parts of the lungs. Knowledge of these conditions has been considerably increased by operations under local anesthesia, in which it was found that the parietal and diaphragmatic pleuræ are sensitive to pain everywhere while the visceral pleura possesses only a few sensitive areas (44). Tem-



perature and tactile sense are entirely absent. Pain sensations of the parietal pleura can be differentiated from those of the skin (Hoffmann). The costal pleura seems to be the most sensitive part, for a mere touch quickly leads to blood pressure changes resulting from the pain which ensues. The lung parenchyma itself is insensitive to pain, the same is true of the branches of the pulmonary artery, and the distal ends of the bronchi, but cutting through the larger bronchi in man induces collapse. The pleura is also said to be able to induce cough reflexly (45). In fact, a sudden spasmodic, irrepressible cough is seen frequently in paracentesis or rib resection for empyema. Kohts (cited by Staehelin 46) has been able to induce cough from the pleura experimentally, and according to Frankel, a coughing spell can be produced in patients with pleuritis by light pressure on the intercostal spaces.

According to experiments performed by Langendorff and Zander, and also by Cordier (cited by Zesas), the pleural reflex is supposed to depend on the vagus, and does not occur after it is cut. V. Saar could demonstrate that it is caused chiefly by stimulation of the pleural parietes (with exception of the diaphragm). According to prevalent opinion it is due to a mild, but long lasting form of pleural reflex in pleuritis, that contraction of the intercostal muscles takes place, which leads to the pulling in of the side of the chest. The rigidity of the abdominal walls in this disease is also considered a result of reflex action.

How this supposed pleural reflex causes the sudden death in open pneumothorax must remain undecided for the present. A similar death occurs if one of the main bronchi is suddenly occluded. Lichtheim (5) in his verification of the experiments of Traube, observed that the lung becomes markedly distended and hyperemic when the main bronchus is obstructed. This might also obstruct the healthy lung, in which case these sudden deaths could be considered due to insufficient respiration.

Dyspnea with open pneumothorax probably has no connection with the pleural reflex; at least it occurs in a similar manner when the vagus has been previously cut (Sackur). The elimination of one lung does not suffice to explain the condition, since it is known that in a resting individual with one-tenth of the respiratory surface active, no dyspnea occurs (Hofbauer). There must be insufficient oxygenation of the venous pulmonary blood, for the oxygen content of the carotid blood falls considerably early in pneumothorax (Sackur, Bruns). In long continued cases, this diminished oxygen content of the carotid blood is not so marked; it may even become normal after strenuous respiration, although it must be recognized that the blood flow through the collapsed lung is probably diminished. Sauerbruch, on the other hand, takes the stand, as stated above, that the collapsed lung is better supplied with blood than the distended lung; and

since the blood cannot be oxygenated in the former but must take up all its supply from the latter, it follows that the total arterial blood leaving the lungs is a mixture of oxygenated and non-oxygenated blood. We have already discussed this conception critically, and can only add that, according to general clinical experience, a closed unilateral pneumothorax does not cause the severe discomfort produced by an open one. Quite the contrary, tuberculous patients with their operative pneumothorax, are comparatively comfortable.

The dyspnea with open pneumothorax, cannot then be explained by the elimination of the function of one collapsed lung, but resides in the fact that the healthy lung cannot perform its function perfectly with its partner in this condition. It is hindered first by a mediastinal flutter, and then by the "pendulum-air" (Brauer). This means that with every expiration, air is forced into the collapsed lung and with every inspiration is rebreathed into the healthy lung. Naturally, this air is soon used up and prevents sufficient fresh air from entering the normal lung.

These respiratory disturbances here described are the chief symptoms in the disease picture of *pneumothorax*. In open pneumothorax they assume such an importance that the occurrence of this condition must be absolutely avoided. Fortunately not every small opening produces an instant complete pneumothorax as in the cadaver; but that from a moderately large opening becomes complete only after several inspirations (see p. 442) (47).

The disturbances in the greater circulation are due chiefly to the fact that the increased pressure in the right ventricle and in the large veins disturbs the sucking up of the venous blood (Sauerbruch).

At the time of its occurrence, there may be a passing pressure increase in the greater circulation, but as the experiments of Friedrich have shown, this pressure depends on the pressure within the pulmonary arteries (44).

Experiments made in low pressure chambers showed that with the increase of the extrapulmonic pressure, the pressure in the pulmonary artery is also increased, and *vice versa*.

Consequent to the decrease in the pressure differences between the bronchial tree and the pleura, the resistance in the lesser circulation is increased, which in turn produces an hypertrophy of the right ventricle, which can be demonstrated experimentally as well as clinically (37), (48). The flow of venous blood into the right heart may likewise be impeded, and this explains the cyanosis of such patients. Then, must be added, that through kinking of the mediastinum, the large vessels are mechanically displaced, and the low position of the diaphragm impedes the outflow of the inferior vena cava.

Nevertheless, clinical experience has shown that these circulatory disturbances assume dangerous proportions only with a pre-existing weakened myocardium. Hartl (99) has placed the body under higher pressure, and the head under normal pressure, and then studied these influences on the blood distribution. By this experimental procedure, the blood is forced into the lesser circulation, and blood pressure rises, a finding which might eventually be utilized in hemorrhage.

If it is the removal of the pressure differences between the bronchial tree and the lung surface which leads to these severe disturbances, readjusting this pressure difference, either by increasing the pressure in the bronchial tree (increased pressure) or diminishing the pressure over the lung surface should remove these dangers (decreased pressure) (50). Frequent controversy resulted over the question of whether increased and decreased pressure were physiologically similar (51). According to the critical work of Burckhardt (14), this must be admitted absolutely for the stationary condition of the pressure difference, but by the introduction of the differentiation process, they are not similar. Schlesinger (52) in lung extirpations, has repeatedly obtained pneumothorax in the unoperated side. The cause is not quite clear, but he believes it is due to the higher pressure, because Sauerbruch and Robinson (53) saw nothing similar with decreased pressure. Robinson frequently observed a pleuritis in lung extirpation under increased pressure, which he interprets by saying that the cavity produced under high pressure conditions possesses normal air pressure, and that, therefore, the organ of the other side does not push over as quickly as it does with the decreased pressure procedure.

How far such a distended lung participates in gas exchange, *i.e.*, in the actual respiratory process, is not as yet clear (Friedrich (44)). Of course, it does not perform respiratory movements.

A closed pneumothorax is frequently produced operatively in the treatment of pulmonary tuberculosis. The disturbances caused by this condition are, according to the above statement, slight. It promotes healing of the tuberculosis, first, by collapsing cavities which gives them a better chance to cicatrize. Furthermore, it is hoped that a functional rest of the lung can be obtained and thereby influence the inflammatory process favorably. Actually, complete rest is not possible, because, as stated above, the lungs as a whole are moved constantly to and fro by the pendulum air and the oscillations of the mediastinum. These movements are even more pronounced after extrapleural thoracoplasty, at least if the radical operation has been performed, and in the beginning, conditions are similar to those of open pneumothorax. Pendulum air and mediastinal flutter are so pronounced that the operated lung is bulged forward with each inspiration, and pulled back with each expiration ("paradox respi-

ration") (53). But even if a pneumothorax or thoracoplasty does not place the lungs completely at rest, they lead to functional rest at least, since actual respiratory movements decrease or cease almost entirely.

Furthermore, in pneumothorax and thoracoplasty, connective tissue grows rapidly and by encapsulating tuberculous foci, is an able curative factor (54). The cause of the connective tissue growth is not entirely understood, but Sauerbruch is of the opinion that functional rest leads to the formation of connective tissue, just as we know it in other tissues, *e.g.*, muscle. Furthermore, the lymph stasis which occurs in these collapsed lungs is a supposed factor, for Shingu (55) showed that soot collects in the connective tissue and the lymph nodes of collapsed lungs, but in the alveoli and bronchi of the breathing lung. In pathological anatomical investigations, the lymph channels were found dilated (Kostler).

Nor is it clear how much the circulatory changes favor connective tissue formation, especially since authors, as stated above, are by no means of united opinion in regard to the blood supply of the collapsed lung (56). We only know at present that connective tissue formation has been observed following ligation of both the pulmonary arteries and the pulmonary veins (57). But it is difficult to say which is the primary factor, functional elimination of the lung or the circulatory changes. To add to the confusion, Bruns (37) found such connective tissue growth experimentally not only in a collapsed diseased lung, but also in a collapsed healthy organ.

The process by which the cavity of a pneumothorax is obliterated differs from that in the expansion of the fetal lung. Roser (58) disproved the oldest view, *viz.*, that the cavity was filled by granulation tissue just as in other deep wounds, in that the lung expands after operation for empyema and fills the pleural cavity. As investigations of others have shown, a distention of the bronchus occurs before distention of the lung, but even if the increased pressure in the bronchial tree is not sufficient to explain the expansion, it does become great enough during coughing and abdominal compression to overcome the elastic forces of the lung (19,) (17), (59), (45). It is the custom to favor this distention by allowing the patient to blow up air cushions, into bottles, etc. as soon as possible. But the air continuously flowing in through the opening in the chest opposes these efforts.

Reineboth investigated the advisability of changing the size of this opening in order to influence distention but he found it made no difference. The advice of Schede and Thiesssch to prevent inflow of air as far as possible by an airtight bandage, or by attaching a valve to the drainage tube is of more practical importance. Perthes's suction apparatus works on the same principle.



As *x*-ray pictures have shown, redistention of a lung always begins at the hilus (60). Roser and Bouvertt point out that this redistention is also favored, *i.e.*, recollapse is prevented, by the presence of adhesions between both pleural surfaces, and this idea seems reasonable. Finally, the cavity decreases also because the mediastinum is pulled over from the other side, the diaphragm becomes elevated, and the ribs sink inward.

After complete removal of a lung, the resulting cavity is obliterated, not only by the organs in the vicinity, including the heart, the other lung, the mediastinum and the diaphragm, but also by the bony thoracic wall which adapts itself to this dead space in a very short time. In experimental animals, the ribs flattened themselves from the angle towards the sternum, so that in a few weeks the whole cavity created by the removal of the lung, was completely filled up (61).

In *exudative pleuritis*, the conditions are somewhat different, in spite of the similarity to closed pneumothorax it otherwise has. First, it must be recognized that the exudate is under peculiar physical conditions. The fluid occupies a horizontal position only when air is present in the pleural cavity, usually it is driven very high on the lateral pleural wall because of the irregular negative pressure in the pleural space. Thus it does not collect at the lowest point simply by gravity. If the pressure is measured in puncturing pleuritic exudates, as is often done, it is always found to be negative, provided that the height of the level of the fluid is taken into consideration (62). The negative pressure is explainable by the compensatory enlargement of the thorax. This enlargement is not passive, but active; it involves not only the diseased, but also the healthy side of the chest. If the power of the inspiratory muscles fail, severe compression symptoms with circulatory disturbances may suddenly occur (62). These latter are, as a whole, similar to those of closed pneumothorax, but are more severe for two reasons, the fluid cannot be compressed, and its weight is greater than that of air. Consequently the changes in the activities of the mediastinum and the diaphragm are much more pronounced in exudates, and the danger of a kinking of the vessels is greater. The characteristic death seen in large pleuritic exudates has been related to this kinking of the lower vena cava (63). This death is very sudden and errors in prognosis are easily made. The removal of the exudate should, therefore, not be delayed too long.

Notwithstanding the compensatory enlargement of the chest cavity, the exudate exerts pressure on the lung surface, as evidenced by the development of circumscribed atelectatic areas. In larger exudates, the weight of the fluid column is sufficient to explain the atelectasis even if the pressure at the upper margin of the fluid is negative, as explained above; but in smaller exudates, the explanation is more difficult. O. Rosenbach

(19) speaks of a change in the pulmonary tonus, which might mean that the capillary attraction between the two pleural surfaces is suspended in localized areas, and at these places the elasticity of the lung would be the predominant force.

These circumscribed atelectases hinder oxygenation because the blood flows through portions of the lung which are not aerated, but in pleuritis the alteration in breathing with its diaphragmatic and circulatory disturbances probably depends primarily on the pain during inspiration. The work of Siebeck, Bittorf and Forschbach (64) gives information on this subject.

These various disturbances may be entirely absent when the exudate is encapsulated (see Clairmont a.o. (65)).

A special type of operative lung compression is the diaphragmatic paralysis produced by cutting of the phrenic nerve (66). Apart from its elevated position on the paralyzed side, a "paradox" movement of the muscle occurs, since it does not descend, but is pulled upwards like a collapsed sail during each inspiration. In bilateral paralysis, the impediment to respiration may be severe enough to cause dyspnea on slightest exertion. After phrenic nerve section no change which might be interpreted as due to compression, can be demonstrated in a normal lung (Schepelmann).

The type of dyspnea seen in ascites, large ovarian tumors, pregnancy, etc., is also due to the pathological position and function of the diaphragm, which is forced upward and impeded in its movements. The ribs are occasionally elevated on account of the abdominal distention, and this adds to the trouble by bringing them into the inspiratory position.

Quite different in many ways to lung compressing processes, is a condition included under the name of *emphysema* in which both the chest and the lungs are enlarged. It is an open question whether "chronic interstitial pulmonary emphysema" is etiologically a distinct disease. Pronounced cases of dyspnea show at autopsy enlargement of the alveoli and atrophy of the interalveolar tissue. The cause of dyspnea is the decreased vital capacity of the lungs (see Siebeck). In a certain sense, the thorax assumes the inspiratory position permanently, but the movements are handicapped in both directions. The thoracic enlargement also flattens the diaphragm (67). Bronchial catarrh is a complication which makes it difficult in a given case to decide how much of the dyspnea is due to the emphysema, and how much to the bronchitis. The hypertrophy of the right heart is usually interpreted, without further question, as an expression of the increased resistance in the lesser circulation. This latter is perhaps partly due to the diminished calibre of the vessels from the marked inspiratory position (see above), but the experiments of Licht-

heim (31) cited above, oppose this view. He showed that the blood pressure remains entirely unchanged in both the greater and lesser circulation when the pulmonary artery is ligated, so that narrowing of the blood channels alone cannot explain the hypertrophy of the right heart. These experiments have been confirmed by Gerhardt, but the results were qualified by showing that they apply only when the body is at rest, while during activity, even a slight narrowing of blood channels in the lungs offers resistance to the heart.

Furthermore, the chronic cough of these patients also occasions a pressure increase in the lesser circulation. Up to the moment when the glottis opens, the air in the bronchi is strongly compressed while the thorax struggles to assume the inspiratory position. The increased pressure in the bronchial tree, and the pressure exerted by the ribs clash during the coughing spell. This leads to such marked compression of the vessels within the lungs, as Gerhardt could demonstrate, that the pressure falls even in the carotids. The *x*-rays show that the heart becomes smaller during the pressure test of Valsalva, which points to the fact that it receives less blood from the lungs. Then to this must be added that numerous capillaries are destroyed along with the pressure atrophy of lung tissue. Furthermore, in emphysema the normal pump action of the respiratory excursions is absent. This must be chiefly responsible for the venous stasis in emphysematous patients, to which must again be added, in relation to the lower extremities, that the low position of the diaphragm compresses the inferior vena cava (30). Numerous differences in detail occur in the individual cases of this common disease. Even if an emphysematous patient can be recognized from the barrel-chest, short neck with distended veins, impeded respiration with physical exertion, and cyanosis of face and neck, there are still individuals with overdistention of the lungs who do not belong to this class.

Two factors are observed so regularly in emphysema, *viz.*, overdistention of the lungs, and altered excursions of the thorax, that it seems reasonable to see in either one of these changes the cause for the other, inasmuch as overdistention of the lungs would bring the thorax into the inspiratory position, and conversely, the inspiratory position of the thorax overdistends the lungs. W. A. Freund (68), as is well known, has shown in his anatomical investigations that the rib cartilages display a "yellow degeneration;" they increase in length, but lose their elasticity. Calcification of the cartilages appears. This lengthening of the ribs, which may amount to 1.2 cm., lifts the chest, and forces the ribs into the inspiratory position. These cases would represent those in which primary changes in the chest wall have produced an overdistention of the lungs as a secondary consequence. Puncture of the ribs, palpation, and *x*-ray

pictures have all shown that these changes in the cartilage occur quite frequently, so that the recognition of a separate disease picture is probably justified.

The findings of W. A. Freund have been verified by v. Hansemann, but are disputed by Sumita (69).

If, notwithstanding the findings in the costal cartilages, there is still doubt that this is actually the primary change, the improvement which appears immediately after operation, according to the uniform statements of all authors, proves that the least the rigidity of the thorax does is to render the suffering much more intense (70). Of other changes in the thoracic wall leading to fixation in the inspiratory position, must be mentioned the arthritic changes in the costo-vertebral articulations (71), and the kyphosis in senile spondylarthritis, described by Loeschke (71). In this kyphosis, the ribs above the hump are in the inspiratory position, and those below in the expiratory position. Similar malpositions of the ribs are also found in tuberculous spondylitis. Finally, Wilms (51) (Schenker) claims that this inspiratory position in emphysema is caused by spasm of the respiratory musculature, because they are under increased nerve tonus, and he believes he has demonstrated an hypertrophy of these muscles.

The second group of authors hold that the primary factor in emphysema is the overdistention of the lungs. Of course, the secondary thoracic enlargement cannot be due to "a mechanical pressure," exerted by the lungs on the thoracic wall, for their strength is not sufficient.

The primary enlargement of the lungs may be due to "dynamic causes," as they are called, *i.e.*, the lung loses its elasticity (Virchow), or to "mechanical" disturbances, such as chronic bronchitis with cough or asthma (72). Numerous examples may be found in support of both possibilities, and in the majority of cases it is probably impossible to take a decided stand. Eppinger and Hess (73) bring the emphysema of youthful individuals in relation to vagotony. They believe that an increased tonus of the bronchial musculature is present in such patients, and it makes expiration more difficult. For information concerning the bronchial musculature itself, see Lohmann and Muller (74).

It would lead too far astray to discuss single cases, like the vicarious emphysema which results when larger portions of the lungs are rendered useless, or that due to unusual exertions (for instance, unaccustomed mountain climbing, etc.), since they have less interest for the surgeon, but the emphysema due to narrowing of the respiratory passages must be considered. It may follow goiters, mediastinal tumors, even obstruction of the nasal passages. Cervells (70) saw lung distention in dogs, whose nostrils had been completely closed. Kuhn (46) who caused a dog to



breathe for a long period of time through his suction mask, also found emphysema; likewise Ludsucki who operatively narrowed the trachea in rabbits. Hirtz, Koehler and Schall performed similar experiments (75).

The cause of this distention is to be found in the deeper inspiration than expiration which follows stenosis. Inspiratory dyspnea is produced, and thus the mean capacity is increased. This occurs in acute stenosis (*i.e.*, we find marginal emphysema in the drowned, or in the asphyxia deaths from blood aspiration), as well as in chronic stenosis (see later). Strenuous expiration alone does not lead to emphysema (76).

It is easily understood how lung distention is exceptionally favored during coughing or compression, and therefore, chronic bronchitis is almost universally considered one of the chief causes of pulmonary emphysema. Occupational factors, such as blowing wind instruments, lead to emphysema, or, probably more accurately, to an increase of the residual air, since it is undecided whether this is true emphysema or not. Undoubtedly, not all persons subjected to similar causes will develop the disease (76) and it seems necessary to assume that there is a certain predisposition in some patients.

Ribbert (77) points out, that the enlarged bronchioles themselves, by compressing the larger bronchi, are a purely mechanical obstruction to the emptying of the air.

The changes in respiration caused by *chronic narrowing of the respiratory passages* (*e.g.*, by goitre, etc.), were first studied experimentally by Koehler (78). It was shown that slight narrowing leads to deeper inspiration, so that no deficiency in oxygenation occurs, on the contrary, the alveolar air often contains less carbon dioxide than normally, and the carotid blood does not contain more. Since expiration is not increased proportionally, the mean capacity of the lungs must be increased when the air channels are narrowed, and thus there is a tendency to emphysema. This greater inspiration often does not compensate during more strenuous muscular exertion, and then goiter patients complain of dyspnea. They are also in great danger when the breathing surface is diminished by pneumonia; during which disease compensation may fail. In high grade stenoses, the equilibrium is not maintained even during rest, and the patient finally dies of asphyxia, if not from previous failure of the damaged heart.

In *acute asphyxia*, accumulated carbon dioxide is the first substance to make itself felt, anesthetizing the patient after a preliminary stage of excitement; then the results of oxygen deficiency dominate the picture with convulsions, dilatation of the pupils, and respiratory failure. The heart stops later. But as long as it beats, recovery is possible, and there-

fore artificial respiration must be used persistently. In this condition, the chest is fixed in a deep inspiratory position and the patient endeavors to increase inspiration still more. The pressure of the air in the pleural cavity is constantly diminished and the skin of the flanks is pulled in. The explanation of the cyanosis still offers great difficulty in such respiratory obstructions, but it seems quite reasonable to suppose that blood changes occur. It is known that discoloration of the blood is caused, not by accumulation of carbon dioxide, but by decrease of oxygen, yet decrease of oxygen is not present during the cyanotic stage of asphyxia. During anæsthesia, as every surgeon knows, it is not uncommon to see the blood suddenly become darker as soon as a slight excess of anesthetic is administered, or respiratory hindrance occurs. In this form of cyanosis, discoloration of the blood doubtless occurs, but the oxygen and carbon dioxide content during the asphyxia are not known.

The *club fingers* often seen in chronic chest conditions offer a problem of either congestion or some form of nerve alteration. There is a certain analogy to acromegaly, but changes in the hypophysis are by no means always present. The report of Klauser (79), who observed marked club fingers with a shoulder luxation of long standing, without a sign of congestion in the arm, but with a paralysis of the hand, shows that injuries to the peripheral nerves may lead to these peculiar changes.

We have discussed the *blood distribution* and its changes during breathing and after operative pneumothorax and we may now briefly review other conditions which also effect it. Changes in the position of the body, as for instance the elevation of the pelvis, during operation have a decided influence on the blood supply. When the pelvis is elevated, a much heavier blood column rests on the heart and may readily cause acute dilatation, as Trendelenburg (80) among others, could show with the *x*-rays. For this reason, and also because of changes in the cerebral circulation, this position should not be maintained for much longer than 10 minutes, unless very necessary. We must also bear in mind the severe acute change in the blood distribution after such operative interferences as the temporary compression of the aorta and the pulmonary artery necessary in the Trendelenburg (81) operation for removal of pulmonary emboli. Lawen and Sievers (82) carried out such experiments on animals, in which they made accurate observations of the heart action, blood pressure and pulse. They found that the heart can withstand a compression of the aorta and the pulmonary arteries for six minutes and still recover. Compression of the superior vena cava was much more dangerous; after three minutes cerebral symptoms made their appearance. That the conditions in man are similar has been shown in operative cases in which by Trendelenburg's method, removal of pulmonary emboli was attempted

(83). The conditions following compression of the abdominal aorta as required in Momburg's belt, are far less damaging to the heart.

Of all embolic processes, *i.e.*, the carrying of blood clots or foreign substances through the blood channels to different organs of the body, *pulmonary emboli* with their frequent fatal results, hold the chief interest for the surgeon. Therefore, the whole question of embolism is best discussed here.

The pathological physiological consequences are greatly dependent on the sort of material deposited, *i.e.*, fat, air or blood clot.

Emboli of blood clot presuppose thrombus formation in some part of the body, knowledge we owe to the first work of Virchow (84) which still remains the classic. The great majority of all thrombi carried to the lungs originate in the veins of the leg; their cause, and the experiments concerning them will be discussed later. Why a thrombus, which, of course, often develops without previous embolism should become suddenly detached, is not known. A diminution of heart action, which is of great importance in the further transport of emboli, probably does not cause detachment of a clot, neither is there anything known of the fermentative processes which cause softening of a thrombus with some degree of regularity.

Such an embolus of blood clot reaches the lung through the right heart and the pulmonary artery. If small, it leads to an atelectatic area, which can become the seat of secondary inflammation. If it is large, it quickly leads to heart failure and asphyxia with compression of the pulmonary artery, as in the experiments of Lawen and Sievers (82) mentioned above. It is not necessary to describe in detail the interesting pathological anatomical findings which occur in lung infarction since they are of no surgical interest.

Another very essential question, for the comprehension of embolism, has been carefully studied; and this is the retrograde transport of solid particles through the blood channels (85). Such a backflow occurs when two currents of unequal size mix. The force of one of the currents may be strong enough to fill the mutual stem only temporarily, but it will at once produce a retrograde movement in the weaker current (86). Such pressure fluctuations in the veins are in close relation to respiration, and especially to sudden changes in the intrathoracic pressure, as, *e.g.*, in coughing (87), asphyxia, etc. Ernst (88) thus describes a retrograde embolism which was possibly the result of artificial respiration, and he points to similar possibilities in chloroform anaesthesia. Experimentally, it was found that foreign bodies of low specific gravity are often driven far into the veins of the extremities (89). According to the observations of Ribbert *in vivo*, and the experiments with models (90), these foreign

bodies are carried chiefly in the marginal current of the veins. Retrograde transport of large emboli, however, cannot be due to a gradual backflow as Ernst believes, but must be from a sudden strong power reversing the current.

With open foramen ovale, thrombi may pass from the right to the left heart, and then into the arterial circulation, where they may produce embolic occlusion of vessels, especially in the brain (paradox-embolism). But it has been proven absolutely by the experiments of Teutschlander that the old idea of O. Weber (91) is correct, *viz.*, that very small clots can pass through the pulmonary circulation. Teutschlander traced particles of India ink from the leg veins of an animal into its cerebral arteries. But it must be a very minute particle, such as India ink granules, or isolated bacteria, or it will not pass through the pulmonary circulation. If larger emboli are found in the greater circulation it must be supposed that either there is an open foramen ovale, or an endocarditis, or a vessel with thrombi on its wall. Such clots circulating in the greater circulation may, of course, reach any organ and produce infarction. At present these arterial emboli are of interest to the surgeon, only if occurring in the extremities, since, in this case, their operative removal is often successful, and a limb otherwise lost can be saved (92).

Fat globules (93) are undoubtedly the most frequent emboli. Ever since Zenker described the first case, this very satisfactory experimental subject has been thoroughly examined, especially from the surgical viewpoint. The fat enters the veins chiefly from the bone marrow when it is loosened by any kind of injury, and it is then carried by the venous blood to the heart and from there to the lungs. The injury may be very slight; according to Ribbert tapping the tibia with a hammer suffices; indeed Fritsche could find fat in the lungs of perfectly healthy rabbits. Possibly in this case, the agitation of the bones from chasing the animals and their occasional impact against the cage was sufficient. Fat emboli in eclampsia can be attributed to a similar slight trauma (Virchow), but such small quantities of fat are of no clinical importance (94). Large masses are, however, very much so. They appear frequently after fractures in older people, and especially if considerable concussion was caused by the accident, for instance, in a fall from a great height. The reason why old persons show this tendency is that their bone marrow is more fatty and richer in oleic acid, *i.e.*, more fluid as age advances.

The fat gains entrance first into the veins of the bone marrow, and from there into the lesser circulation, but there is also absorption through the lymph channels, by which it is carried through the thoracic duct into the greater circulation. In the investigations of Fritsche who produced fractures after ligating all the veins in the legs of rabbits, it seems in



severe bloody fractures the fat was taken up by the blood vessels, while in milder breaks the lymph channels were favored. According to Reiner (95) its transport by the blood can be observed directly before the Esmark bandage is removed, if a cannula is tied into the saphenous vein after orthopedic operations in a bloodless field. Fat globules are mixed with the blood, but Lexer could not verify this statement. We have often found fat in the venous blood of the traumatized limb immediately after a severe injury.

Riedel obtained fat emboli through the lymphatics by injecting oil into the abdominal cavity. Fat emboli from other organs, for instance, the subcutaneous tissue, are of far less importance than those from the bone marrow (Grondahl), although in the first case described (Zenker), the fat came from the liver. Fat embolism also occurs from inflammatory processes in fat containing organs, especially from osteomyelitis, while there is little danger from burns, toxemias and general metabolic disturbances. It is thought that fat absorption in osteomyelitis is favored by the liquefaction incident to the inflammatory process.

In a broader clinical sense, fat embolism of the lesser circulation must be differentiated from that of the greater circulation (96). Since, as stated, the fat reaches the right heart through the veins, the question arises of how it can enter the greater circulation at all. An open foramen ovale is not always present, and the fat must necessarily pass through the lungs (97). It is possible that this is favored by the forced respiration which occurs when the fat first occludes the pulmonary artery. At any rate, as Virchow pointed out, the passage of fat from the lesser into the greater circulation is a complex process. Groendahl performed an experiment with a rabbit in which he injected oil, then removed a kidney, then made a pneumothorax, and finally extirpated the other kidney, after which he found that the second kidney contained very much more fat than the first. He concludes that an essential factor for the passage of fat is the extent of the pulmonary vascular area, but this experiment permits of another interpretation. According to the same author, the diameter of the pulmonary vessels is not important, but we may assume that the quantity of the fat circulating in the blood cannot be ignored.

A large number of cases in which fat emboli are found in the lungs at autopsy show no clinical symptoms, and respiratory disturbances occur only when a larger number of pulmonary capillaries are occluded. Pathologically anatomically, edema and capillary hemorrhages are found, both of which probably increase the respiratory difficulties. The marginal emphysema, usually observed, must be considered due to this impeded respiration, but the reason for the irritative cough which often develops immediately after the embolism is not clear (98). It is also

unknown whether a preceding fat embolism favors inflammatory processes in the lungs (pneumonia after fractures in the aged).

In the pulmonary vessels, a part of the fat is saponified by the alkaline blood serum and thus prepared for absorption (Beneke (99)); another part is taken up as fat droplets by the vessel endothelium. The remainder passes through the lungs, as stated above, and appears in the greater circulation.

Theoretically, it may be distributed among all the organs, but practically, the brain is the only one of serious importance. According to Grondahl, the fat remains in this organ because there is an exceptionally large blood supply flowing through small capillaries which are presumably less capable of dilatation. But slight nutritional disturbances in the brain are also quickly detectable clinically. It is characteristic of cerebral fat embolism that it does not occur immediately after injury probably because the fat is retained at first in the lungs. For this reason, pulmonary symptoms often precede brain symptoms. The latter consist of lessened threshold to pain (Czerny), restlessness, anxiety, increased temperature, numbness and paralyses, and must be considered as true localized symptoms. Increased brain pressure has not as yet been observed, probably because cerebral reactions (lymphstasis, etc.) develop slowly.

The fat may pass the capillaries of the greater circulation as well, and be eliminated in the urine.

Air embolism (100) occurs through the sucking in of air into an open vein. This presupposes that the venous pressure is low, or actually negative, which is especially true of the veins close to the heart. This low pressure is still further decreased by a previous loss of blood (101). By using excess or negative pressure anesthesia, this danger of the entrance of air can be greatly reduced (102). On the other hand, an excess pressure in the thorax is obtained by abdominal compression during anesthesia, by which a retrograde transport of air through the veins is possible (88). We observed a case in which an area of softening in the brain occurred from this accident following a goiter operation. A similar case was described by Van de Kamp (103).

Furthermore, the veins must gap in order to permit the entrance of air, and, therefore, veins passing out through spaces in the fascia are especially endangered, as well as those which are superimposed on a tumor (*e.g.*, goiter) and thus pressed flat.

Air embolism is more dangerous than fat embolism, because an air bubble acts like a valve in blood vessels and interrupts the blood stream. It is only necessary to recall what occurs when an air bubble is enclosed in an irrigator tube to appreciate the conditions. It is not quite clearly

understood where this interruption of the circulation, in other words, the cause of death, takes place. The only fact known is that in experimental air embolism a measurable quantity of air is found in the right heart, and it is possible to keep the animal alive in a certain percentage of cases by sucking out this air (104). Whether death occurs because the right heart is unable to press the contained air bubbles out (105), *i.e.*, cannot contract sufficiently, thus interrupting the blood supply to the lungs, or whether the air occludes the pulmonary capillaries has not been definitely settled at present. Perhaps both causes operate, and the form of death depends on the rapidity of the entrance of the air. Passage of air from the lesser into the greater circulation occurs only in occasional instances. Air bubbles are rarely found in the brain and the old theory of Bichat of "brain death" from air embolism is abandoned.

The case is different when air is injected into the arteries, or enters the portal circulation, in which latter case it must pass through the liver (see Wolf). Here the bubbles are broken into minute globules which pass without obstructing capillaries. Wolf always found air not only in the femoral vein after its injection into the femoral artery, but also scattered throughout the whole circulation. The death resulting is then probably a "brain death." Clairmont (65) describes a clinical case of arterial air embolism in a patient with opened interlobar empyema. Embolism occurred during a change of dressings.

As stated, much depends on the rapidity with which air enters; Wolf could inject 100 to 200 c.c. slowly without causing death. It may be assumed that a large part of the air is quickly liberated through the lungs, and it is of interest, conversely, that experimental air embolism may be produced by blowing air into the trachea (106). It is not known whether most things similar has been observed during the use of the excess pressure method, unless the observation of Schlesinger (cited on p. 383) is interpreted in this way. The various animals used in these experiments are by no means equally sensitive to this procedure (104).

A special form is seen in divers who are released too quickly into the air from a high-pressure diving bell. During the rapid decrease of pressure, gas is liberated from the blood cells (107) and there are minute air globules scattered everywhere in the vessels. Of course, puncture of the heart to liberate the air does not help in these cases.

As already stated, postoperative lung complications are the causes of the greatest number of deaths after operation (108). Investigations have shown that they may be due to many factors, and have a most varying pathological basis. First, there are *postoperative pneumonias* which are due entirely to the anesthesia, and for a while ether was considered very dangerous for the lungs (109), (108). This question was approached

experimentally, and the difference in results depends chiefly on the concentration of ether or chloroform which comes in contact with the lungs. Poppert, who worked with a rather concentrated ether and chloroform vapor, came to the conclusion that the injury, especially from ether, is quite considerable. But Holscher obtained no changes in the lungs, except a slight hypersecretion of the bronchial mucous glands. Lichtenberg found scattered atelectasis and emphysema of the edges after anesthesia of long duration. If the animals were killed 24 to 48 hours after the anesthesia was concluded, pneumonic infiltration and true bronchopneumonia could be demonstrated. Offergeld (110) arrived at similar results.

It can well be realized that a lung injured by anesthesia is especially liable to infection, but how do infective organisms reach the lungs? Durck's (111) investigations have shown, in the first place, that the normal lung is not free of bacteria. During anesthesia, they may enter the smaller bronchi from the mouth by aspiration, as was shown by Holscher in animals. He placed solutions of dyes in the mouths of anesthetized animals, and after longer anesthesia could find the dye, together with mucus, in the deeper bronchi, but this flow did not take place if the animal had been anesthetized with the head hanging downward. Aspiration of the contents of the mouth could also be avoided by turning the head sideways, cleaning the mouth of mucus, etc., precautions which should, therefore, be considered as very essential. The experiments of Holscher, to discover if anesthesia injured the ciliated epithelium, resulted in negative findings.

[After their experimental experience with war gases, Winternitz and his collaborators were led to investigate the lymphatics of the trachea and larger bronchi. It was found that the submucosa of the trachea contains a very rich plexus of lymphatics which anastomose with similar channels in the bronchi at the bifurcation, and these in turn communicate with lymphatics of the smaller bronchi, and so on. Infection (pneumococci), introduced into the lumen of the trachea by needle puncture or by insufflation, spread via these lymphatics to the lung, provided the epithelium of the trachea was damaged. But these lymphatics are also protective, in that most of the drainage from the trachea and bronchi flows into the regional lymph nodes. The possibility of a direct pathway is present, however, and this may well be utilized in certain postoperative lung infections (112).]

Anesthesia furthermore reduces the immunity of the organism as a whole to bacteria. Snel (113) injected anthrax bacilli into the lungs of anesthetized frogs. While normal frogs are immune and do not react to this injection, anesthetized animals developed anthrax pneumonia and died.



As stated above, after anesthesia, small hemorrhages can frequently be demonstrated in the lungs, a proof of circulatory disturbance. But the latter may result after operation quite independent of anesthesia, *i.e.*, from insufficient aeration, from painful abdominal incisions, or from a high position of the diaphragm, as for instance, in peritonitis. Heart disturbances, which often depend on anesthesia, may also lead to such circulatory changes. The net result is hypostasis, or a local pulmonary edema, and this especially favors the development of pneumonia.

A further injury, to which patients are exposed during all operations, is chilling; and its influence on the lungs has been investigated by Henle and Heile (114) who poured ether over anesthetized rabbits, and noted a marked fall in the temperature of the body. The lungs showed hyperemia, hemorrhages, and injury to the alveolar epithelium. In all these cases the anesthesia was of very short duration.

Embolism constitutes one of the most severe circulatory disturbances of the lungs, as stated above. Pneumonia, caused by fat emboli, is occasionally seen after fractures; postoperatively it is more likely to be due to small embolic blood clots. Gebele (115), in 40 animals, obtained 12 cases of pulmonary embolism by means of varied operative procedures (*i.e.*, ligation of the larger abdominal vessels, handling of bowel, etc.). In the presence of emboli, naturally, pathogenic organisms may reach the lungs and a pneumonia is the certain result.

But pathogenic organisms enter the lungs by the lymph channels far more frequently than in blood clots. Goebel (116) investigated this question by injecting the intestinal wall with bacteria and India ink, after which he found these particles in the pulmonary lymph vessels. Lymph channel connections between the lungs and the abdominal cavity have often been demonstrated anatomically (117). Tillmann (118) and v. Lichtenberg point out that this, perhaps, explains the comparatively large number of cases of pneumonia following ulcerative processes in the stomach and intestines. Nevertheless, great care must be exercised in drawing too far reaching deductions of the clinical picture of post-operative pneumonia from the fact that isolated bacteria are experimentally carried through the lymph channels. The chest and the abdominal cavity, notwithstanding the numerous lymph tracts between them, are in fact two distinctly separate regions, as is proved over and over again by rarely finding an empyema with peritonitis, and *vice versa*. At the same time the anatomical relations are especially favorable for infection of the pleura from the peritoneum. The pleura, indeed, just as the peritoneum, has a certain immunity to pathogenic organisms. According to the investigations of Notzel, it is necessary to inject three to four times the quantity of bacteria

into the pleura to kill an animal as compared to the quantity required in subcutaneous or intravenous injection (119).

It can be seen from the extensive literature regarding pneumonia after contusion of the lungs, that trauma itself may cause post-operative pneumonia or bronchitis (120). It is supposed the injuries produce small hemorrhages in the lung tissue, or at least, that the vitality of the lung tissue is diminished. Finally, as Chiari (121) points out, nervous disturbances of the bronchi similar to those in asthma, *i.e.*, changes in the secretion of the mucous membranes, incited by the trauma, must be added as causative factors.

#### LITERATURE TO LUNGS

1. Minkowski: in Krehl-Marchand, "Allgemeine Pathologie," V. 2, 1. Bittorf-ibid., Stahelin in Mohr-Stahelin's "Handbuch d. inneren Med.," V. 2. Garre-Quinke Lungchirurgie, 2 Edition. Sauerbruch in Handbuch d. prakt. Chir. Rosenbach, Nothnagel's Handbuch, 14.
2. Bohr: Skandinav. Arch. f. Physiol., 1890, V. 2.
3. Krogh: Skandinav. Arch. f. Physiol., 1910, V. 25.
3. Du Bois Reymond: Arch. f. Physiol., 1910.
4. Haldane and Douglas: Skandinav. Arch. f. Physiol., 1911, V. 25.
5. Traube: Gesammelte Beitr. zur Physiologie u. Pathologie, V. 1. Lichtheim: Arch. f. exp. Path. u. Pharm., V. 10. Hofbauer: Ztschrft. f. klin. Med., 1907, V. 61.
6. Sauerbruch: Mitteil. a. d. Grenzgebieten, 1904, V. 13. Friedrich: Arch. f. Klin. Chir., 1907, V. 82, p. 1147.
7. Fick: Arch. f. Anat., 1897 (Suppl.).
8. Magnus: Ergebn. d. Physiol., 1902, V. 1.
9. Pribram: Wiener klin. Wochenschrft., 1918, V. 48. Sturtz: Deutsche med. Wochenschrft., 1911, p. 2224. Sauerbruch: Deutsche med. Wochenschrft., 1913, p. 625.
10. Henzelmann: Wiener klin. Wochenschrft., 1918, p. 1340.
11. Wenkebach: v. Volkmann's Sammlung klin. Vort., No. 140-141. Hofbauer: Zentralbl. f. Klin. Med., 1905.
12. Tendeloo: Studien uber d. Ursachen d. Lungen krankheiten. Wiesbaden, 1901-1902 and Ergebn. d. Inneren. Med., 1910, V. 6.
13. West: Brit. Med. Journ., 1887. Brauer: Ziegl. Beitr. z. pathol. Anat., 1905, V. 7, suppl.
14. Burkhardt: Bruns Beitr., 1918, v. 110; Chirurgenkongress, 1914.
15. Keller: Pflugers Arch., 1879, V. 20, p. 365.
16. Hermann: Handbuch d. Physiologie.
17. Reineboth: Deutsches Arch. f. klin. Med., 1897, V. 58.
18. Stovesand: Arch. f. exp. Path. u. Pharm., V. 65.
19. Rosenbach: Notnagel's Handbuch, V. 14.
20. Skzreczka: Maschka's Handbuch d. ger. med., 1881, V. 1., p. 855.
21. Siebeck: Deutsches Arch. f. Klin. Med., V. 93. Hasselbach: Deutsches Arch. f. Klin. Med., V. 93.
22. Hering and Brener: Wiener Akademie, 1808.
23. Einthoven: Pfluger's Arch. f. d. ges. Physiol., V. 124.

24. Fredericq: Arch. de Biol., 1900-1901.
25. Hesselbach: Biochem. Zeitschrift, 1912, V. 46.
26. Scott, R. W.: "Significance of undissociated carbon dioxide in Resp." Am. J. Phys., 1918, 47, 143; "Production of intracellular acidity by carbon dioxide," Am. J. Phys., 1920, 53, 547.
26. Reimann, S. P., Bloom, G. H. and Reimann, H. A.: "Administration of CO<sub>2</sub> after anesthesia and operation," J. A. M. A., 1921, 76, 437.
26. Jacobs, M. N.: "To what extent are physiolog. effects of carbon dioxide due to H ions?" Am. J. Phys., 1920, 51, 321. Henderson, Y., Haggard, H. W. and Coburn, R. C.: "Therapeutic use of CO<sub>2</sub> after anesthesia and operation," J. A. M. A., 1920, 74, 783. Barcroft, J.: "The Respiratory Function of the blood," Cambridge Univ. Press, 1914, Lancet., 1920, 199, 485.
27. Hofbauer: Wien. klin. Wochenschrft., 1902. Hasse: Arch. f. Anat., 1906.
28. Brauer-Roth: Beitr. zur Klinik. d. Tuberkulose, V. 4. Brauer: Munchener med. Wochenschrft., 1910, p. 2169. Bruns: Habilitationsschrft. Marburg, 1909; Beitr. z. Klinik d. Tuberkulose, V. 13.
29. Ledderhose: Mitteil. a. d. Grenzgebieten, 1905, V. 15.
30. Eppinger and Hofbauer: Ztschrft. f. klin. Med., V. 72.
31. Lichtheim: "Die Storungen des Lungenkreislaufs" Arch. f. exp. Pathol. u. Pharm., Berlin, 1876, 10.
32. Tigerstedt: Skand. Arch. f. Physiol., 1902, 14. Gerhardt: Ztschrft. f. klin. Med., 1904, V. 55 and Arch. f. exp. Path. u. Pharm., 1908 (suppl.).
33. Ebert: Arch. f. exp. Path. u. Pharm., 1914, V. 75.
34. Sackur: Ztschrft. f. klin. Med., 1896, V. 29.
35. Brauer: Beitr. z. Klinik d. Tuberkulose, V. 12 and Mitt. a. d. Grenz., 1906, V. 13, Marv. Univ. Prog.
36. Cloett: Arch. f. exp. Path. and Pharm., V. 66 and V. 70; Chirurgenkongress, 1912.
37. Bruns: Beitr. z. Klinik. d. Tuberkulose, V. 12.
38. Propping: Arch. f. Klin. Chir., 1919, V. 112.
39. Lohmann and Muller: Sitzungsber. d. Ges. z. Bef. d. Ges. Naturwissenschaften zu Marburg, 1913.
40. Romanoff: Arch. f. exp. Path. u. Pharm., 1911, V. 64.
41. Brauer: Deutsche Ztschrft. f. Nervenheilkunde, V. 45.
42. Zesas: Deutsche Ztschrft. f. Chir., 1912, V. 119. v. Saar: Chirurgenkongress, 1912. Petersen: Grenzgebiete, V. 26.
43. Dogiel: Arch. f. mikrosk. Anat., 1903, V. 62.
44. Hoffman: Naturhist. Med. Verein. Heidelberg, 1919. Friedrich: Arch. f. Klin. Chir., V. 82, p. 1160.
45. Gerhard: Deutsche Chir., 1892, Lief. 43.
46. Staehelin: Jahreskurse f. arztl. Fortbildung Februar heft, 1914.
47. Reineboth: Deutsches Arch. f. Klin. Med., V. 58.
48. Hirsch: Deutsches Arch. f. klin. Med., V. 64 and 68.
49. Hartl: Beitr. z. Klinik. d. Tuberkulose, V. 12.
50. Sauerbruch: Bruns Beitrage, V. 76 and 79. Brauer: Mitteil. a. d. Grenzgebieten, V. 13.
51. Sauerbruch: Ergeb. d. Chir., 1911, V. 2. Tiegel: Mitteil. a. d. Grenz. 3 Suppl. Seidel: Grenzgebiete, V. 17. Garre-Quincke Lungechirurgie, Fischers Verlag, 2 edition.
52. Sclesinger: Arch. f. Klin. Chir., V. 95.
53. Robinson: Deutsche Ztschrft. f. Chir., V. 102. Sauerbruch: Ergebn. d. inn. Med. 1913, V. 10.

54. Muralt: Munchener Med. Wochenschrft., 1909, V. 50. Kistler: Beitr. z. Klinik. d. Tuberkulose, V. 19. Gratz: Beitr. z. Klinik. d. Tuberkulose, 1908, V. 14.
55. Shingu: Beitr. z. Klinik. d. Tuberkulose, 1908, V. 11.
56. Bruns-Sauerbruch: Mitteil. a. d. Grenzgebieten, V. 23.
57. Tiegel: Arch. f. klin. Chir., V. 95.
58. Roser: Berliner klin. Wochenschrft., 1878.
59. Schede: Deutsche med. Wochenschrft., 1885. Weissgerber: Berliner klin. Wochenschrft., 1879.
59. Bouveret: cited by Reineboth.
60. Jochmann: Ztschrft. f. Elektrotherapie, 1906. H. Curschmann: Physik. u. Med. Monatshefte, 1904.
61. Friedrich: Arch. f. Klin. Chir., V. 87, part 3.
62. Gerhardt: Deutsches Arch. f. Klin. Med., V. 92. Weitz: Arch. f. exp. Path. and Pharm. Festschrft, for Schmiedeberg.
63. Eppinger: Allgem. u. spez. Pathol. d. Zwerchfells Wien, 1911.
64. Bittorf and Forschbach: Ztschrft. f. Klin. Med., V. 70. Sieback: Deutsches Arch. f. Klin. Med., V. 100.
65. Clairmont: Arch. f. klin. Chir., 1919, V. 111.
66. Schepelmann: Arch. f. klin. Chir., 1913, V. 100, p. 985. Sturtz: Deutsche med. Wochenschrft, 1911-1912. Sauerbruch: Munchener med. Wchenschrft., 1913, V. 12.
67. Hofbauer: Erg. d. inn. Med., 1909, V. 4.
68. W. A. Freund: Beitr. z. Histologie d. Rippenknorpel, Berlin, 1898. Der Zusammenhang gewisser Lungenkrankheiten mit primaren Rippenknorpelanomalien Erlangen, 1859. Arch. f. klin. Chir., V. 92. Chirurgenkongress, 1910.
69. v. Hansemann: Arch. f. klin. Chir., V. 92. Sumita: Deutsche Ztschrft. f. Chir., V. 113.
70. Seidel: Bruns Beitrage, 1908, V. 58. Hoffman: Zentralbl. f. Chir., 1909. Friedrich: 39 Chirurgenkongress.
71. v. Salis: Frankf. Ztschrft. f. Pathol., 1910, V. 4. Loeschke: Deutsche med. Wchenschrft., 1911.
72. F. A. Hoffman: "Emphysem. u. Atelektase" in Notnagel's Handbuch, V. 14.
73. Eppenger and Hess: "Die Vagotonie," by Noorden Samml. klin. Abh., 1910.
74. Lohmann and Muller: Sitzungsbericht. d. Gez. z. Bef. d. ges. Naturwissensch. z. Marburg, 1912.
75. Schall: Beitr. z. Klinik. d. Tuberkulose, V. 14.
75. Hirtz: These de Paris, 1878. Kohler: Arch. f. exp. Pathol. u. Pharm., V. 7.
76. Prettin and Leibkind: Munchener med. Wchenschrft., 1904.
77. Ribbert: Virch. Arch., 1916, V. 221.
78. Morawitz and Siebeck: Deutsches Arch. f. klin. Med., V. 97.
79. Klauser: Munch. med. Wochenschr., 1912, p. 929.
80. Trendelenberg: Prakt. Ergebnisse d. Geburtshilfe u. Gynakol, 1912.
81. Trendelenberg: Arch. f. Klin. Chir., 1908.
82. Lawen and Sievers: Deutsche Ztschrft. f. Chir., V. 94.
83. Sievers: Deutsche Ztschrft. f. Chir., V. 93. Trendelenberg: Deutsche med. Wchenschrft., 1908 and Arch. f. klin. Chir., 1908.
84. Virchow: Frorieps Notizen, 1846.
85. v. Recklinghausen: Virch. Arch., v. 100.
86. Beneke: Marchand-Krehl, "Handbuch d. allg. Pathol.," V. 2, 2.
87. Heller: Deutsche Arch. f. Klin. Med., V. 7.



88. Ernst: Virch. Arch., V. 151.
89. Ribberts: Zentralbl. f. Pathol., 1897. Arnold: Virch. Arch., V. 124. Risel: Virch. Arch., V. 182. Frerichs: Klinik. d. Leberkrankheiten, 1858, V. 2.
90. Bouma: Virch. Arch., V. 151.
91. O. Weber: Pitha Billroth Handbuch d. Allg. Chir., V. 1, p. 87. Teutschlander: Naturhist. med. Verein. Heidelberg, 1916.
92. Matti: Konespondenzblatt. f. Schweizer Arzte, 1913.
93. Busch (lit.): Virch. Arch., V. 35, Riedel, Deutsch. Zeitschrft. f. Chir. v. 8, Virchow in Virch. Arch., V. 5. Tromberg Grenzgeb., 26; Fritsche, Deutsche Ztschrft. f. Chir., V. 107, Grondahl; Deutsche Ztschrft. f. Chir., V. 111. Busse Korrespondenzblatt. f. Schweizer Arzte, 1913, Reiner, Munchener, med. Wchschrft. 1907-1, Ribbert, Deutsche med. Wchschrft., 1900, Beneke, Ziegler's Beitr., 22 Werzejewki, 10 Kong, Deutsch. Gess. f. 4, 465 Orthopadie (discussion here).
94. Schmorl: Uber Puerperaleklampsie, Leipzig, 1893.
95. Reiner: 10 Orthopadenkongress.
96. Payr: Ztschrft. f. Orthopad Chir., V. 26.
97. Busse: Korrespondenzblatt. f. Schweizer, Arzte, 1913. Tromberg: Mitt. a. d. Grenzgebieten, V. 26.
98. Fibiger: Compare Grohndahl, l. c.
99. Beneke: Ziegler's Beitr., V. 22.
100. Wolf (Luftembolie): Virch. Arch., 1903, V. 174 further Beneke, in Marchand-Krehl, "Allg. Path." 2, 2.
101. Becker: Ztschrft. f. Medizinalbeamte, 1911.
102. Tiegel: Chirurgenkongress, 1912.
103. Van de Kamp: Dissert. Munchen, 1913.
104. Kleinschmidt: Chirurgenkongress, 1912. Jehn and Naegeli: Ztschrft. f. d. Ges. exp. Med., 1918, V. 6.
105. Cohnheim: Allg. Pathol., 1877, V. 1.
106. Beneke: Arch. f. Entw.-Mech., 1910, V. 33. Marchand: Vierteljahrsschrft. f. prakt. Heilkunde, 1876, V. 33.
107. Hoppe-Seyler: Muller's Arch. f. Physiol., 1852.
108. W. Lichtenberg: Zentralbl. f. d. Grenzgebiete, 1908, V. 11; Bruns Beitrage, V. 57; Munchener Med. Wchschrft., 1909.
109. Lowit: Ziegl. Beitrage, V. 14. Stursberg: Mitteil. a. d. Grenzgebieten, V. 22, p. 11. Poppert: Deutsche med. Wchschrft., 1894 and 1897, Deutsche Ztschrft. f. Chir., V. 67. Lengemann: Bruns Beitrage, 1900, V. 27. Lindemann: Zentralbl. f. path. Anat., V. 11. Holscher: Arch. f. Klin. Chir., V. 57, p. 175.
110. Offergeld: Arch. f. Klin. Chir., V. 75.
111. Durck: Munchener med. Wochenschrft., 1904.
112. Winternitz, M. C., Smith, G. H., Robinson, E. S.: "Pathway for bacterial invasion of resp. tract," Bull. J. Hopkin's Hosp., 1920, 31, 163.
113. Snel: Ztschrft. f. Hyg. u. Infektionskrankheiten, V. 40.
114. Henle and Heile: Arch. f. klin. Chir., V. 64; Chirurgenkongress, 1901.
115. Gebele: Bruns Beitrage, V. 43.
116. Goebel: Mitt. a. d. Grenz., V. 18.
117. Kelling: Chirurgenkongress, 1905. Kuttner: Bruns Beitrage, V. 14. Franke: Deutsche Ztschrft. f. Chir., V. 119.
118. Tillman: 15 Internat. Med. Kongr. Lissabon, 1906.
119. Notzels: Bruns Beitrage, V. 46.
120. Stern: for lit. Traumat. Enst. inneren Krankheiten, Jena, 1910. Venus: Zentralblatt. f. d. Grenzgebiete, 1909.

121. Chiari: Bruns Beitrage, V. 81.
122. Georg Fischer: Arch. f. klin. Chir., V. 9, p. 571.
123. Barth: Schriften d. Naturforscher-Gess. in Danzig, 1902, V. 10.
124. Kronecker and Schmey: Deutsche med. Wchenschrft., 1884, p. 364.
125. Rose: Deutsche Ztschrft. f. Chir., V. 20, p. 319.
126. Cohnheim: Allg. Pathologie, 2 edition, 1882, p. 21. Riegel: Deutsches Arch. f. klin. Med., 1882, V. 31, p. 471. Placzek: Vierteljahrsschrift f. ger. Med., 1902. Lewis: Journ. of Phys., 1908, p. 233.
127. Molitoris: Wiener klin. Wochenschrft., 1919, p. 868.
128. Sauerbruch: Arch. f. klin. Chir., V. 83.
129. Elsberg: Bruns Beitrage z. klin. Chir., V. 25, p. 426. Bode: Bruns Beitrage z. klin. Chir., V. 19, p. 167.
130. Rehn: Arch. f. klin. Chir., 1897, V. 55.
131. Michaelis: Ztschrft. f. klin. Med., V. 24, p. 270. Frey: 10 Kongr. f. innere Med., 1891. Porter: Journ. Physiol., V. 15. Panum: Virch. Arch., V. 25, p. 308.
132. Laewen: Munchener med. Wchenschrft., 1919, p. 5.
133. Kolb: for lit. Berlin Klin. Wchenschrft., 1913. Brauer: Arch. f. Klin. Chir., V. 71.
134. Goringstein: Bruns Beitr. z. klin. Chir., V. 86, p. 229.
135. Heidenhain: Deutsche Ztschrft. f. Chir., V. 41. Schuster: Ztschrft. f. Heilkunde, 1880, p. 417.
136. Barie: Revue de medicine, 1881, p. 132.
137. Bohm: Mitt. a.d. Grenzgebieten, 1914, V. 27, p. 567.
138. Leporski: cited in Chirurgenkongress-Zentralblatt, V. 4, p. 151.

## CHAPTER XI

### BRAIN AND SPINAL CORD

In the great majority of surgical diseases of the brain and its membranes, the symptom complex, known as "*increased pressure*" plays the foremost role (1). To this belong headaches, slowing of the pulse, choked disc, unconsciousness, convulsions, respiratory paralysis and similar symptoms. They are incited when there is a disproportion in the contents of the skull and its capacity, whether it be that the vault of the skull is driven into the brain, as in a depressed fracture, and the space is decreased, or whether it be a swelling of the brain against the resistance of the unyielding walls of the skull. In both cases there results a pressure on nerve cells, and this mechanical irritation in the form of injury of the nerve cells leads to the above mentioned symptoms. Recently, Reichardt (2) measured the relation between the capacity of the skull and the volume of the brain, and secured figures which show that an increase of brain volume plays a large role in the establishment of "*increased brain pressure*" and, for example, in brain tumors without hydrocephalus, the brain volume is still increased even after removal of the tumor.

Since the various parts of the brain differ in their functions, it is obvious that pressure on the motor area of the cortex must give different manifestations than pressure on the medulla oblongata. But these local effects are not as difficult to understand as the general symptoms, which appear in greater or less degree in all cases, but do not seem to follow pressure on any special part. The older theories (1), (3) sought an explanation in a factor which would affect the whole brain equally, that is, in disturbances of circulation. These theories, principally, through the influence of v. Bergmann and Kocher, have so dominated the literature, that disturbances of the brain cells on which symptoms of brain pressure must depend in the final analysis, have been relegated to the background, even though attention was called quite early to the onesidedness of such theories (4). But not only the experimental results, but also the experience gained at operations have emphasized the consideration of brain pressure as "*a mechanical injury to nerve tissue*" (1), (5). The circulatory disturbances are supposed not to alter nutrition but merely to afford a possibility for a compression of the nervous elements (Hauptmann). This appears to be the other extreme; for circulatory disturbances may not be entirely guiltless in the production of brain pressure symptoms.

The peculiarity of the circulation of the brain lies in the fact that this organ is enclosed in a non-yielding capsule. It cannot, therefore, become enlarged like other organs, and an increase in fluid content from passive congestion or from increased arterial flow, leads to brain pressure symptoms. It is not the blood vascular system alone which plays a part in its circulatory phenomena, but the cerebral circulation is still further complicated by the presence of *cerebrospinal fluid*. According to newer opinions, the physiological purpose of this fluid is "to provide a mechanical safeguard for the centers and a regulatory mechanism for the blood supply of the brain" (6). The brain literally swims in this fluid. It is not to be compared casually to lymph, for it lacks the nutritive substances which the lymph carries. According to Mestrezat (7) there is no noteworthy mixing of lymph and fluid, even in the perivascular spaces.

Its origin is by no means understood (8). That it is no simple transudate from the blood is certain from its chemical composition, for it contains more crystalloids than blood serum. On the other hand, secretory stimulants, such as pilocarpin, increase its pressure. Whether it is secreted from the choroid plexus only or from the "vessels and substance of the nervous system" also (9) is still uncertain, although newer investigations seem to show that the cells of the brain and spinal cord are also concerned. Bungart (10) resected and ligated the subarachnoid space of the spinal cord of animals in two places and allowed the isolated space to empty itself. After 12 hours it was again filled with fluid. Clinical observations in the sacculated meningitis of fractures of the vertebræ have indicated that the fluid is formed in all parts of the central nervous system. This question is of surgical importance, because in hydrocephalus, attempts have been made to destroy the source of the abnormal formation of fluid by removal of the choroid plexus (11). This procedure is rational only, of course, if the choroid plexus is principally at fault.

Its chemical composition is also of surgical interest, because the large number of lumbar punctures for spinal anesthesia in patients with healthy central nervous systems have supplied normal fluids for analysis. The statement that 1 per cent. of albumen is normal (Riecken and others) has been found incorrect (Bungart). Ordinarily, only the very faintest trace is present, but even a slight stimulus leads to an increase. Thus Bungart, in patients who had trouble after spinal anesthesia, found albumen in a second puncture fluid when none had been present in the first. The irritation in this case was chemical. Larger amounts with leucocytes, occur in bacterial inflammations (infections), but in addition, slowly progressing chronic conditions, particularly late syphilitic inflammations, such as tabes and paresis, lead to pathological albuminous bodies in the fluid



which can in general be recognized only after precipitation with ammonium sulphate (12).

The quantity which can be produced, especially in gunshot wounds when the ventricles are opened, is well known to surgeons; although in this case, it is doubtful if the conditions are normal. Nau and Hermann (13) showed that the fluid in the lumbar region would return to its original pressure in 20 minutes, when a large quantity had previously been removed.

The fluid flows into the cerebral veins, partly by way of the Pacchionian bodies and partly through the perivascular lymph spaces. Some, however, flows toward the lymph vessels of the neck, as Hill and Ziegler (14) have determined by the injection of dyes. Furthermore, the subarachnoid space is in communication with the sheaths of peripheral nerves, as Bungart (10) has shown by strychnin injections, and this latter fact is of extreme importance in the spread of tetanus.

Increase of pressure leads to increased absorption (3) and this mechanism functions so smoothly that there need be no fear of increased brain pressure during the induction of spinal anesthesia. The procedure of allowing a considerable amount of fluid to flow out before injection of the anesthetic is superfluous.

The fluid is present both in the subarachnoid space and in the ventricles, but it has lately been questioned whether this system of canals is really one unit, *i.e.*, if the fluid in the ventricles communicates with the fluid in the subarachnoid space through the foramen of Magendie and other openings. Schmorl (15) showed that in icterus, the subarachnoid fluid, but not that in the ventricles, was discolored. Conversely, other substances do not pass from the fluid in the ventricles to the cerebrospinal fluid. The question of whether there really is a foramen of Magendie in humans, is of therapeutic interest. For, until now, we have thought that a lumbar puncture in hydrocephalus also empties the ventricles and that their fluid escaped through the foramen of Magendie into the subarachnoid. There have even been extensive operations on the spinal column designed to allow a lengthy drainage of fluid from the ventricles in hydrocephalus. Furthermore, it was thought that acute hydrocephalus often arose as a result of the closure of the foramen of Magendie through inflammatory products. The findings of Schmorl are so consistent, however, that it seems better to consider our opinions of hydrocephalus and its therapy by lumbar puncture incorrect. This necessitates the view that the flow of fluid in general is so small, that it is reabsorbed in practically the same place it was formed. But this is refuted by Schmorl himself, who observed an icteric color in the subarachnoid fluid as soon as the ependym of the choroid plexus was injured.

In practical surgery, this conclusion may be drawn from Schmorl's findings. In all cases of dilatation of the ventricles, and in the different varieties of hydrocephalus, it is a more physiological proceeding to practice methods of direct drainage of the ventricular fluid, such as puncture of the ventricles, the Anton-v. Bramann puncture of the corpus callosum, ventricular drainage, etc.

The subarachnoid space is so completely separated from the subdural space that even easily diffusible poisons do not pass the boundaries, as Bungart (10) has shown.

The question of whether there is a flow of liquid in the cerebrospinal fluid itself, ignoring the debatable communication with the ventricles, has been the subject of repeated investigations. The current plays a definite part in spinal anesthesia, and it is thus accepted on experimental and observational grounds, but the results of injecting dye particles (16) must not be applied to humans without further knowledge, both on account of the different posture of the body and anatomical differences. The observation of Propping (17) that there were symptoms of paralysis of the region of the medulla oblongata in a half hour after a spinal anesthesia with tropakolain is in the last analysis an infrequent event, from which we can draw conclusions regarding the normal flow of fluid only with the greatest caution. According to Reichmann we have at present no definite proof that a flow really occurs and yet the findings of Graf Haller, that nodding movements of the head increase the pressure by 10 cm. of water or more, seem to show a sort of pumping of the fluid which is carried backward into a cistern at the end of the fourth ventricle, and indicates the presence of a current (18).

The pressure factors in the subarachnoid space have been studied not only on the living and on cadavers, but also on models (19). The latter are not all alike, since Grashey conceives the vertebral canal as a container with rigid walls and Propping, more correctly, considers it somewhat elastic by reason of the fat and veins in the epidural space. In a sitting posture, the fluid pressure is not zero at the foramen magnum occipitale, but at about the upper thoracic vertebræ (20), so that, as Propping showed, puncture between the atlas and occipital bone allows air to be sucked into the vertebral canal. These models do not accurately imitate the relations in the living subject, for in the latter, while reclining, there is a pressure of from 1 to 12 cm. of water, while it is zero in a cadaver. This may be related to the tension of the tissues, particularly the dura mater.

Not only are pulse beats and respiratory movements transmitted to the fluid, but congestion in the large veins of the neck is registered on the manometer.

If we now return to a consideration of circulatory factors in the production of brain pressure, we can expect, theoretically, an increase through conditions in the arterial, venous and cerebrospinal fluids (21). But these three factors are so adjustable that increase of one leads to a diminution of the other. Since Burrow's (22) time, therefore, we speak of a constant content of the skull, rather than the constant quantity of blood, as in the older description of Monroe who disregarded the fluid entirely. Leyden (23) increased the cerebrospinal fluid by the injection of egg albumen into the subarachnoid space and all the symptoms of acute brain pressure resulted. If the blood pressure was lowered simultaneously the symptoms were manifested so much the earlier.

He argued that the entrance of the symptoms depends on anemia of the brain. This same thought lies at the basis of the work of others (3), (24) who, in general, produced brain pressure, not by increasing the quantity of fluid, but by pressure over the cerebral cortex. They found, uniformly, that these manifestations appear only when the pressure exerted on the brain is increased above the blood pressure, and further that experimental cerebral anemia through ligation, or embolic occlusion leads to exactly the same signs (3). Finally, Cushing demonstrated that these phenomena appear when the pressure and the coincident anemia are slowly increased, and persist until the anemia becomes sufficient to stimulate the vasomotor center and cause more blood to be brought to the brain through a general rise of blood pressure. This has great practical significance, because through Breslauer (5) we find in acute brain pressure (*e.g.*, in fracture of the skull), an increased blood pressure, even before the typical symptoms such as slowing of the pulse, etc., are distinct. The presence of this increased blood pressure is explainable by these experiments of Cushing.

The correctness of these observations is beyond doubt, but their interpretation is not quite clear. Sauerbruch and Hauptmann, by producing pressure on the brain and simultaneously recording the blood pressure, have shown that the behavior of the pulse and respiration does not change even when the circulatory factors of the brain have again become normal. By this it can be deduced that the symptoms are not entirely dependent on circulatory disturbances, but are also influenced by injury to the nerve cells, either through pressure *per se*, or secondarily, through the intimately connected circulatory disorders. We must think as Geigel, that these latter cannot be judged simply by autopsy findings, since they depend not so much on the quantity of collected blood, but on how much oxygenated blood was flowing through the capillaries, and how it was distributed. Brain pressure symptoms may also be present, therefore, without anemia (5).

If pressure is exerted on the brain, venous obstruction occurs first, *i.e.*, passive congestion; tighter compression will involve the arteries with subsequent anemia. Through passage of fluid toward the vertebral canal the effects are diminished at first; soon, however, the cerebellum closes the foramen magnum and its full influence is exerted on the brain itself.

Following such a circumscribed pressure are found the umbilications, whose presence has not been explained, despite numerous investigations (6), (25). Forcing out of the tissue fluids certainly plays a part, for von Albert and Schnitzler observed an increased flow of brain fluid from a cannula tied in the sheath of the optic nerve, when they increased the brain pressure. Besides this, the pressure on the vessels and cells may cause this umbilication. However, the question does not seem to merit the significance that has been attached to it.

At all events, it follows from this discussion that a correlation between fluid pressure and brain pressure is not to be expected without further evidence. No certain conclusions can be drawn from the pressure of the fluid obtained by lumbar puncture. But not infrequently in diseases or injuries which are partners to brain pressure, there is an increase of fluid in the vertebral canal and in the ventricles, which on puncture flows out under increased pressure. A congestion in the venous circulation seems to be the best explanation for this "hydrocephalus," for congestion would offer obstruction to the absorption of fluid (26). On the contrary, however, Breslauer, in researches on this subject, never produced an hydrocephalus in animals by ligation of the vena magna Galeni or of the veins of the neck, nor had he better success by mechanical compression of the aqueduct of Sylvius.

For a conception that an acute hydrocephalus follows interruption of the communications of the foramen Magendi, see above in the text, the places of formation and the means of egress of the fluid.

Passive congestion alone, therefore, cannot lead to increase of fluid. The circumstances are as complicated as in ascites, in which it is often necessary to assume the presence of an inflammatory factor. According to the investigations of Finkelburg (27), an increased formation of fluid follows alcohol poisoning, and this author believes the headache after a revel with Bacchus is due to an acute hydrocephalus. Tumors may act on the brain similarly through unknown chemical substances, or by mechanical injuries (see Reichardt (2)).

It is not unlikely that these secondary changes determine the differences between experimental and clinical brain pressure, particularly the chronic variety which we see in our patients. All these researches on animals



give us knowledge only of what is happening during a short time interval as we allow a pressure of measured intensity to act.

In our patients, however, conditions are different, insofar as certain lasting injuries have been instantly inflicted by the pressure on the delicate nerve cells; if the pressure continues for a longer time, as in brain tumors or in unredressed depressed fractures, a whole series of later disturbances cloud the picture.

It is unessential whether we ascribe these secondary complications to toxins or inflammation, or something else, it is essential that we regard them as an indication of an increase in the combined contents of the skull (2). The pathology itself is brought about by these complications in a reduced space, and it is toward this space reduction that we must direct our therapy. Since, therefore, this secondary swelling of the brain (Breslauer) involves the entire organ, it follows that these same symptoms will be called forth secondarily by pressure on, or disease of any or all parts of the brain. We have mentioned, as an example, their occurrence after ligation of the arteries (Hill). Further, even when the cerebrospinal fluid has a free means of egress, local decreases of space in the skull may bring about a generalized brain pressure (28). The latter, as has been emphasized before, is independent of pressure conditions in the cerebrospinal fluid.

Therefore, it is always damage to brain cells with especial emphasis on those in the medulla oblongata, which makes so many etiologically different diseases so similar; and the reason for the rapid involvement of the brain as a whole, lies in the anatomical fact of its enclosure in the unyielding cranium, irrespective of the great delicacy and high functional capacity of its cells. In the most widely different diseases of the brain, in tumors, injuries, concussions, inflammations, hydrocephalus, the so-called pseudotumor cerebri, etc. (29), there are always the same general symptoms, such as slowing of pulse, vomiting, faintness, headaches, changes in respiration, increased blood pressure, convulsions and disturbances of consciousness, and pupillary changes (30). The similarity of symptoms does not necessarily point to a similarity of etiology.

Other phenomena to which Breslauer calls attention, arise in large part from pressure on the medulla oblongata. To these belong the disturbances of circulation and respiration, but the cause and location of still other disorders have not yet been found.

It is thought that the seat of consciousness is situated in the cerebral cortex and that disturbances of this sphere (fainting and the like) are due to anemia of this part. Breslauer (31), however, showed in animals that pressure at any place picked out at random on the cortex cerebri, never led to loss of consciousness, but that it did occur with considerable regularity when pressure was increased in the posterior fossa, particularly around the

medulla oblongata. That an injury to the human cerebral cortex does not cause unconsciousness, is well known from war experiences. It is always possible, even if not probable, that these mechanical irritations are not adequate to produce an effect on the cerebral cortex, granting that it is the seat of consciousness. It could be pictured that injuries to the vasomotor center in the medulla oblongata would disturb the function of the cerebral cortex, and with it, consciousness would be abolished.

But it seems to be fairly well established through the investigations of Roy and Sherington (32), Breslau, and others, that the cerebral vessels are not under the influence of the vasomotor center, and that pressure on the medulla oblongata does not lead to anemia. In pharmacological poisonings also, we now assume that there is direct action on nerve cells (33) rather than through circulatory changes. Thus excitement or sleep can both be accompanied by either hyperemia or anemia. Even if it can be said with certainty from the investigations of Breslau that unconsciousness results from injury to the medulla oblongata, it does not follow that all disturbances of consciousness are controlled from this site alone, for hemorrhage in the internal capsule will produce this effect. A definite localization of the seat of consciousness is not possible at present.

A symptom not readily correlated with brain pressure but present in this condition, is choked disc (34). Authors are not in agreement regarding its origin, and its investigation has been pursued chiefly by ophthalmologists. The various theories may be grouped as follows: the mechanical theory, that is, congestion and increased flow of fluid; the inflammation theory, inflammatory products reach the papilla through the fluid; and the neurotropic theory, vasomotor nerve filaments to the papilla are injured by the increased pressure. All of these ideas recognize somewhere the relation of choked disc to brain pressure, and for surgeons, it is necessary only to remember that the relief of the pressure through trephining, will check the progress of the choked disc and improve it. We have learned from the gunshot wounds of the war, that it requires 14 days or longer for a choked disc to develop.

Still another symptom must be mentioned here, *viz.*, dilatation of the pupils. According to the clinical observations and experiments of Hoessly (30) this arises in generalized brain pressure from a centrally originating stimulation of the sympathetic and a decrease of tonus of the oculomotor nerve. There occurs, therefore, not only a paralysis of the basal centers, but also an irritation of the antagonist, namely, the sympathetic. In localized pressure, as for example, hemorrhage from the middle meningeal artery, we frequently see a unilateral dilatation on the side subjected to the pressure (Hoessly), a fact of practical significance.

*Concussion of the brain* (35) follows pressure exerted for a short period

of time, usually from a blow transmitted through the skull. The brain is driven to the opposite side, and wave-like motions scatter themselves throughout the cerebral substance.

The elasticity of the brain should not be undervalued in the application of such force (35), (36). The factors involved have been analyzed both on models and skulls, and it has been found that the skull has an elasticity coefficient between that of a hollow sphere of brass and one of wood. Just as with a sphere, its surface is flattened by the application of a force, and its diameter enlarges longitudinally, vertical to the place struck; for example, a blow across the temples elongates its long diameter and increases its height. If the force is sufficient, a bursting fracture (37) occurs at the instant when it has reached the apex of its described alteration in shape. As a consequence the line of break gapes widely at the time. Since the skull retains its elasticity, even when fractured (v. Bruns), it springs back to its normal form, and during the recoil, it pinches all sorts of tissue, hair, fat, etc., in the line of fracture. If a scalp wound is produced at the same time, foreign bodies such as bits of cloth and portions of the hat or cap may also be included. Needless to say, there is great danger of infection of the brain and its membranes. On account of the vaulted form of the surface of the skull, the pulling forces which are involved in depressing the inner table, are greater than the pressure forces acting on the outer table. The result is that the inner table is usually broken over a wider radius and this increases the danger of compression of the brain. On the other hand, the division into an outer and an inner table acts as an added protection, inasmuch as the external table can be pressed against the inner table without injuring the latter (Tillmann). There is definite damping of the strength of the force. By the same line of reasoning, forces, acting from within outward (gunshot wounds), cause greater injury to the external table (verified by the investigations of Teevan (38)).

The changes undergone in the form of the skull explain the course of the lines of fracture to a certain degree (see also Korber, Bohl and others), but because of its physiological make up, the brain also has a decisive influence which was first recognized in gunshot wounds. If a shot from a modern army rifle at a short distance (about 50 meters) strikes the head, the skull and its contents are completely shattered. By piecing together the splinters it can be seen that both a point of entrance and exit are present; from this it surely follows that the shot passed through one side of the skull before the so-called explosion effect occurred (Tillmann (39)). We are not dealing with hydraulic pressure in this case, that is, the ordinary pressure on the brain, since the explosion must occur when the bullet enters the inner surface of the skull, and it must be assumed that active

forces are transmitted from the bullet to the brain, and that movements of the particles of the brain cause the bursting. This force which the projectile transmits to the brain, and this in turn to the skull, is called a hydrodynamic pressure (40). Experimentally, the same conditions were obtained by shooting through a lead box filled with either water or starch paste, but whether the active forces are transmitted to the human brain, which is, of course, no fluid mass, or only to the fluid and the blood, is difficult to say. The so-called Kronlein (41) shot which causes the brain as a whole to fly out of the shattered skull, seems to indicate that the fluid is the only carrier of the force. According to Mertens (42) a rotary movement of the bullet, imparted by the rifling of the barrel, is necessary for this peculiar explosive act. But the correctness of this view is questioned by Franz (43) who after investigations on bullock brains and human skulls, believes that the results of the Kronlein skull shots are in harmony with the hydrodynamic theory.

That injuries by blows or falls on the head may be increased through the brain is shown by Tillmann's researches on models (36). He struck a glass bulb filled with gelatine and found that the hydraulic pressure broke the globe. The so-called indirect fractures, for example, those of the roof of the orbit, can be explained only through such a transmission of forces (44). These fractures are true contrecoup breaks. Most of those which had formerly been described as contrecoup are produced otherwise according to the investigations of v. Wahl (45), and Messerer (36), *i.e.*, by extension of the other lines of fracture.

The spread of the lines of force in the brain has also been studied on models (36). It was desired to determine how much the brain was mechanically moved by a blow or fall. The researches of Ferrari are particularly instructive. After placing small bits of colored glass in the brain and striking the skull, he found a widespread splintering of the glass bits, even without fracture of the skull itself, provided that the glass was placed no deeper than 5 mm. below the surface of the brain. Felizet, in using paraffin filled skulls, observed an indentation of the paraffin at the place where the blow was struck, and a bulging outward of the opposite side, which is a good illustration of the way the so-called "contrecoup" arises, that is, damage to the cerebral cortex exactly opposite the point on the skull where the blow impinged. The brain, through its change of form and on account of its soft texture, is moved toward the opposite side and may be seriously crushed from the resistance of the bones.

Many attempts have been made to imitate brain concussion; but there resulted either a very severe change which was more than a "concussion of the brain," or no symptoms at all (46). These researches are not entirely meaningless, however, since the fact that the human brain



reacts to even slight concussion with unconsciousness, etc., contrary to the brain of an animal, may be on account of anatomical peculiarities, and because of the higher development of functions in the brain of man. It can be said definitely that all of these acute injuries, concussion, contusion, gunshot wounds, etc., show the same general clinical symptom complex, and differ only in the degree of severity. They probably are alike in their main pathological physiological fundamentals.

This conception was not always the generally accepted one. Since Kocher's time, the phenomena of *commotio-cerebri* have often been looked upon as due to the rapidly occurring anemia. This conception is founded particularly on the investigations of Cushing who allowed saline solution to flow rapidly into the subarachnoid space, after which he found a compression of the veins and then of the arteries. This view was soon disputed by Koch and Filehne. Breslauer also was unable to demonstrate an anemia of the cerebral cortex after all sorts of acute injuries to the brain, so that the foundation of the teaching that pressure anemia of the brain is the cause of the clinical manifestations in concussion, rests on very insecure ground.

According to the work of Koch and Filehne, it is questionable whether the blood supply and its changes are of any importance at all. These authors found in frogs, whose blood vessels had been emptied of blood and filled with saline solution, that hammering of the skull produced changes in the pulse and respiration, analogous to those in *commotio cerebri*. The same *commotio cerebri* with much increased blood pressure, was also obtained in dogs and rabbits by the same procedure. The objection that they are "reflex disturbances" is not valid, even if the conclusions of Massland, Saltikoff (Kocher (35)), and Sauerbruch (47) are not to be doubted, that by blows on the chest and abdomen, such disturbances of respiration and pulse are also obtained.

Quite apart from the purely mechanical changes in the calibre of the vessels in concussion, the blood supply of the brain is, at times, still further compromised by the fact that the vasomotor center itself is involved in the injury. This may lead to very long standing changes in the blood supply of the brain, especially hyperemia, and clinical symptoms, often resembling those of brain tumor, may appear (48).

The symptoms of concussion have often been described as reflex (36), (48), but the length of time that these manifestations continue does not justify this view. However, there is nothing against the view that they are due to direct injury of the ganglion cells especially those in the medulla oblongata. As mentioned above, Breslauer could even relate the presence of the most unexplainable of all the symptoms, unconsciousness, with pressure on the medulla oblongata. Koch and Filehne insist that a blow

on the medulla of animals gives signs which have a marked resemblance to those of brain concussion.

As the pathological anatomical foundation of these injuries to brain cells, descriptions have been given of diffusely scattered blood extravasations (Bright, 1813), and degenerations in the ganglion cells. The fact that the capillary hemorrhages are greater in the gray matter than in the white, is evidence of the correctness of Tillmann's view that the white and gray matter separate because of their different specific gravities (49).

Of great practical interest are the alterations in the vessels which lead to "traumatic secondary apoplexies," (50). Obviously there must be an incomplete tear or injury in a vessel wall, which, after a few days to a few weeks, softens and leads to hemorrhage. A similar event can occur in the very important middle meningeal artery (51). With this possibility in mind, such patients will not be allowed to pass from observation too early, and if secondary hemorrhage occurs—fortunately, it is easily diagnosed—an early operation can be performed.

The *acute inflammations* of the brain and its membranes comprise another group of diseases which may finally lead to brain pressure. Inflammations of the brain substance run a course peculiarly their own. The organ reacts very slowly, and apparently passively to entering irritants, so that it is not customary to see a brain abscess before about the beginning of the second week after injury (52). Fever is often absent; the abscess grows but slowly, and often in periodic advances. A so-called membrane is formed around the abscess, but according to Cassirer (53), this is not in the nature of an actual encapsulation. Hand in hand with this poor resistance, there is a high susceptibility to infection, and in puncturing brain abscesses, great care must be taken to avoid infecting other parts with the needle.

Just as suppuration and inflammation in other tissues are known as abscesses and phlegmons, so in the brain, abscesses are differentiated from encephalitis (54). The limited reactive ability mentioned above, makes the spread of abscesses to encephalitis less common than the spread of abscesses in soft parts to phlegmons. In fact, a brain abscess may be present for years without leading to a progressive encephalitis, and in this respect, the brain resembles bone tissue. There are, however, certain similarities between encephalitis and a phlegmon, for example, in war experiences, brain abscesses frequently were followed by an encephalitis after operative interference. Just as in phlegmons elsewhere, an acute progressive encephalitis may arise a few days after a penetrating wound of the skull without previous abscess formation (52). We observed a fatal diffuse encephalitis following exertion, in an individual who had a small

scar in the brain, from a gunshot wound inflicted a year previously. In other cases, the immediate predisposing cause is not so apparent.

A circumscribed encephalitis may also develop, especially in prolapse of the brain. In animals, Schifone and later Blegvad (55) studied the causes of *brain prolapse*. Anatomical investigations of human cases, date from Schrottenbach (56). With him, we must distinguish the primary prolapse which arises from increased pressure as soon as the bones and dura are separated, from the secondary prolapse which develops a longer or shorter time after trephining, without a heightened brain pressure. Finally, there is a local encephalitis, and in animals, this is observed only when the brain has been injured in some way after the skull is opened. In humans, the study of war wounds has shown that such prolapses disappear, oftentimes very rapidly, with the cessation of inflammation. The impression is gained that this rapidity is not due to organization with connective tissue, and subsequent shrinking, as Schrottenbach believes, but is chiefly due to the removal of inflammatory products, constriction of the dilated vessels, etc.

The danger of meningitis consists in the absorption of toxic substances through the extensive surface of the meninges, until it is no longer compatible with the life of the individual. The patient then dies of the infection. Meningitis leads, also, to an increase of brain pressure, in certain cases from the accumulation of meningeal fluid alone, particularly in the type called *meningitis serosa* first described by Quincke (57). Its peculiarity lies in an aseptic increase in the fluid or in circumscribed or general edema of the meninges. In certain cases, this is a collateral edema, e.g., in inflammations of the skull, head injuries, etc., but there are no grounds for believing that there is any fundamental difference from collateral edema in other parts of the body. It is only because of the paucity of space in the skull that it leads to early brain pressure, and thus to severe general manifestations. This meningitis serosa has also been observed in infectious diseases, in which case a chemical irritant may have interfered with the exchange of fluids. A case of Doenitz (cited by Axhausen (58), illustrates this possibility. A severe purulent aseptic meningitis followed the use of a rubber tube in the connection for spinal anesthesia. In purulent infectious meningitis, the brain pressure symptoms are increased because of changes in the cerebral blood supply, but no detailed investigations of this question seem to have been made.

*Epilepsy* was the first disease of the brain which was subjected to operative interference, at least, skulls from the stone age have been found, which plainly show the smooth opening produced by a trephine, depression fractures in other situations denoting that epilepsy was probably present. In later years (59), even until the last decade, operation for

epilepsy was attempted only after trauma, and thus it came about that a sharp distinction was made between traumatic epilepsy (symptomatic) and one not traumatic (true).

This is not a happy differentiation and epilepsy has lately been considered as a symptom complex (60). Just as in abdominal surgery, the group of symptoms known as ileus arises from all sorts of diseases, so does this symptom complex of epilepsy arise from all sorts of brain diseases and injuries. Unquestionably, this theory has the great advantage of throwing the least number of obstacles in the path of scientific investigation, and when the necessary fundamentals are established through clinical observation and experiments, a suitable classification can be made. Redlich and Binswanger (61) have already devised a grouping into chronic and acute, depending on the number of attacks. This conception seems useful from the therapeutic standpoint.

For the production of an attack of epilepsy, an altered irritability of specialized brain cells is necessary (Binswanger (61)). This is often hereditary and statistics have agreed that about 30 to 40 per cent. (Binswanger), of epileptics have a neuropathic family history. Animals also show differing dispositions. It is much easier to produce an epileptic seizure in guinea-pigs than in dogs; moreover, different animals of the same species differ in their susceptibility. Whether the inherited tendency shows the same and specific changes in all cases, has not been determined, but probably not; at least the anatomical changes which we are accustomed to regard as signs of this disposition differ in individual cases. We often find outspoken signs of degeneracy: webbed fingers, polydactylism, etc. while in other cases there is only an increased irritability of the vegetative system (62). Microscopically, all sorts of changes are found in the brain, sclerosis of the hippocampus major, and so on, *i.e.*, signs of degeneration of the brain itself (63).

In epilepsy, following gunshot wounds of the brain, the Barany test is said to give indications of a general injury of the cerebrum (64). Of special interest, but not as yet answered, is the question of how great a part the secretions of the endocrine glands play in the reactive power of the brain cells, and if then the tendency to epilepsy is in reality an alteration in the internal secretions (Bauer (62)).

As stated, in addition to this predisposition, there is another external factor, so to speak, which arises from trauma, space reducing processes, poisoning, psychical insults, etc. This factor is easier to study experimentally, and a larger number of investigations have been made.

Attempts were also made to discover whether the onset of epileptic attacks was determined by injury to a particular part of the brain; in other words, whether there is a site, or center of epilepsy. The move-



ments during the attacks seem to point to involvement of the motor area in the ascending frontal convolution.

This particular view is supported by the classic studies of Fritsch and Hitzig (65), who discovered that electrical stimulation of this region leads to movements of the opposite extremities and that typical epileptic seizures could be brought about by such stimuli. Studies of the effect of injuries, or electrical or cold stimuli, or the implantation of foreign bodies under the dura have been oftentimes repeated (66). These animal studies in combination with the clinical, anatomical and operative findings of Jackson on humans, have shown that a certain percentage of cases can be cured by the removal of either the stimulated area of the brain cortex, or the cause of irritation. It is not necessary to say that the results of these studies have not shown any special "epileptic center" in the cerebral cortex. Indeed Brown Sequard (66) has shown that in a guinea-pig, injury of different parts of the brain stem, and even of the spinal cord and peripheral nerves was sufficient to incite epileptic seizures when he had removed the combined cerebrum and cerebellum. At the suggestion of Westphal (67), he struck the head of a guinea-pig with a percussion hammer and the decerebrated animal showed immediate convulsive attacks. It is well known, however, that guinea-pigs are easily made epileptic. Brown Sequard reached the conclusion at which Westphal Van Der Kolk arrived, that an epileptic seizure could be compared to the discharge of an electric current, and that it is brought about by a disturbance of the medulla oblongata (68). It might be mentioned that one of the famous decerebrated dogs of Goltz died during a spontaneous epileptic attack.

Nothnagel believed that the "convulsion center" is located in the pons, and was inclined to think with Kussmaul and Tenner, that it is in the floor of the fourth ventricle in relation to the vasomotor center (69). Ziehen (70) found a place in the pons of rabbits which gives rise to tonic convulsions after electrical and mechanical stimulation, and in humans, we know of the tetanic spasms that follow hemorrhage into the ventricle, supposedly from pressure on the brain stem.

On the other hand, Munck showed that a dog which had been made epileptic by long continued irritation of its cortex, still had convulsions after division of the spinal cord. So it must be acknowledged that stimuli for epileptiform seizures can be incited from the cerebral cortex alone.

On the basis of all these investigations, the cortico-medullary theory must be considered the most rational; that is, there is no special part of the brain diseased, but the "discharge" of impulses is related not only to the cerebral cortex, but there is also irritability of the central, "subcortical motor apparatus of the pons and medulla oblongata" (Binswanger). Such a "discharge" apparently may be liberated from any part of the

brain. Knowledge of the organic disease has, therefore, reached this status, and operative procedures, in a certain percentage of cases, have been successful in removing those changes which produce convulsions.

Another aim of the investigative work was to determine what sort of injury would bring forth the attacks. It was stated above, that they may be caused by cerebral injury, especially from pressure following a depressed fracture. It is not difficult to understand this type of long standing mechanical irritation. Doubtless, it will be found that a traumatic etiology occurs more often than is ordinarily supposed. This has been corroborated at autopsy, for in patients with a seemingly genuine epilepsy, definite signs of skull injury have been found consistently. But statistics of peace times, show that the disease had a traumatic origin in only 3 to 15 per cent. of cases.

Other factors have, therefore, been suspected particularly the relation of poisons and toxins to the disease (60). Of the most practical application are the studies on the effects of alcohol, especially absinthe. It is not necessary here to go into the debated question of whether it is the alcohol or the ethereal oil in experimental absinthe epilepsy, which produces the convulsions, but the fact that epileptics are made worse by alcohol is well known (71). The traumatic epilepsy of the war provided a large amount of material for study, especially because it occurred frequently in individuals who were previously healthy and not predisposed to it. It is often surprising to see the attacks resist every form of treatment and then disappear after total abstinence. Like alcohol, lead, also, is harmful. These toxic epilepsies are often differentiated from "true" epilepsy (72) and yet considering our meagre knowledge of the entire subject, it seems that such a division is arbitrary.

From clinical observations (61) and animal experiments also (73), it seems probable that bacterial toxins may cause an epilepsy. Cases of stubborn epileptic attacks in syphilis have been known to disappear after inunctions. Tillmann (74) is inclined to return to the idea of the previous infectious changes in the arachnoid which he saw so often at operation, in cases of genuine epilepsy. These chronic inflammatory changes in the arachnoid may act as irritants to the cerebral cortex, and thus to seizures. Tillmann believes these changes are much more potent irritants than a splinter of bone pressing on the brain, and, therefore, the conclusion follows that the causative mechanisms of traumatic and true epilepsy have much in common and there is no fundamental difference between the two. The extent and distribution of the changes in the arachnoid vary, however, in individual cases, and operative procedures in cases of true epilepsy are more difficult than in traumatic. Further investigations are necessary to show whether these explanations are correct, or whether they are not

just a trifle too simple. Tillmann's statement that these changes in the arachnoid are observable only in the living during operation, and not at autopsy, seems worthy of further observation.

Search has been made for familiar chemical substances which would produce convulsions, but less violent than those of strychnine or tetanus toxin. Landois (75) was successful in applying creatin to the brain surface of animals. This, and other metabolic substances were chosen because epilepsy has been, and still is, regarded by many as a poisoning of the central nervous system, through toxic products of metabolism. This opinion is especially emphasized in French literature (76).

Recently, Sauerbruch (77) produced typical clonic and tonic convulsions in monkeys by the injection of cocain into the blood stream after their cerebral cortex had been injured. The dose necessary was only one-fifth of that which produced convulsions in normal monkeys. This hypersusceptibility increased steadily following the operation until finally twitching of the jaws occurred without the drug. This could also be brought about by means other than operative damage to the brain, as, for example, by producing fatigue of the central nervous system by passive movements of the extremities. By this method, the same phenomenon is obtained as in electrical stimulation of the cerebral cortex, *i.e.*, an ever increasing irritability of brain cells.

Another group of investigations was designed to discover the part played by changes in the blood supply of the brain. It is well known that exsanguinated animals show spasm-like twitchings somewhat similar to epileptic seizures (78). This occurs not only when fowl are butchered, but also in mammals. Similar spasms develop after ligation of the carotids, in which case the poor blood supply, or better, the insufficient oxygen supply, is held responsible. For this reason, convulsions occur when all the cerebral veins are ligated, and the gaseous interchange hindered in this way (79). Sauerbruch (77) studied this subject by varying the pressure applied to the brain and producing alternate anemia and hyperemia in dogs made epileptic with cocain. He was also successful in obtaining repeated epileptic seizures by this method. Care is always necessary in applying the results of these animal experiments to humans, since Bier (80) was never able to bring about an attack in an epileptic by tying a tight band around the neck or by suddenly removing it, and yet Momburg and Eastmann (81) have cured, or at least greatly improved cases of chronic epilepsy by diminishing the calibre of the carotids. The effect of such a slight decrease in circulation is naturally quite different physiologically from the effects of anemia, but it is conceivable that such diminution of blood supply will diminish the irritability of the cells.

The relation of brain pressure to epilepsy has been repeatedly investi-



gated from the surgical standpoint, especially during the attacks, because of the hope of the therapeutic influence of reducing the pressure. Kocher (82) was of the opinion that attacks were brought about by a sudden increase of pressure, and as a matter of fact, Ito found this increase in guinea-pigs. He attributed it to functional hyperemia. But the results of measurements obtained through trephine openings in the skulls of epileptics and non-epileptics, showed such small differences that no conclusions can be drawn from them. Tillmann and Bungart (74) found in a patient who had an epileptic attack following puncture of the ventricle, that the pressure of the ventricular fluid did not rise until the seizure was well established. They concluded from this, that Kocher's idea is incorrect. It must not be forgotten, however, that this case of tumor of the cerebello-pontine angle with secondary hydrocephalus was entirely different, and these seizures must not be compared to true epilepsy without further qualifications. On the other hand, Nowatzki and Arndt (83) found that the brain pressure was normal before, increased only during the first tonic stage, and decreased during the clonic twitchings. After what has been said, it is obvious that the value of this work will not be known until it is settled whether the fluid pressure *per se* gives information of brain pressure. The operative brain findings in true epilepsy give no certain answer to this point. In individual cases, the dura is tightly stretched, the brain is not pulsating or bulging; in other cases, there is nothing indicative of heightened pressure (84). A number are cured or improved by trephining for tension—Mockel reports 25 per cent. cures and 25 per cent. improvement and as many in true as in traumatic epilepsy, but his statistics cover only small series of cases. We do not know if the brain pressure was previously high in these cures, so that the different types of epilepsy differ in this respect, nor do we know what other factors might be concerned in the cure. Wilms (see Mockel) considers the possibility of the escape of some sort of toxic substances through the trephine opening; but this is all conjecture. In animal work, Ito and Mockel thought they could show that trephined animals would not have an epileptic attack as easily as an untrepined one, and that the attacks could be more easily controlled.

Operative surgery of the central nervous system seeks not only to remove the symptoms of general brain pressure, but also to improve local injuries which make their presence known by paralyses. Brain surgery is, therefore, also a "surgery of the motor area" (v. Bergmann). These paralyses originating from local pressure, will entirely or partly disappear if they arise from an extradural hematoma from rupture of the middle meningeal artery. According to v. Bergmann (1), a localized reduction of blood supply is sufficient to abolish the function of the motor area of the



cortex. Pressure continued for a longer time brings about swelling changes in the nerve cells and fibres. Other diseases, such as tumors or cysts following injuries, cause paralyses not only through pressure on the nerve cells, but also by a sort of inflammatory process (see choked disc). The extent and region of paralysis depends on the localization of the disease processes. Animal experiments and operative findings on man have each contributed their share, and our knowledge of the topography of the brain has been much enriched in the last decades (85).

In the nature of things, operative procedures, *per se*, produce a local injury. It should be remembered that in operations in which the corpus striatum is injured locally, there is marked post operative rise of temperature at times (86). Unimportant brain tumors have occasionally produced psychical disturbances of a general type which have disappeared after removal of the tumor (87).

Since there are intracranial sympathetic branches, for example, the ganglion ciliare, or the plexus woven around the cavernous sinus, injuries to these may give rise to hyperalgesic zones in the neck through radiation to the cervical segments. Wilms (88) was the first to draw attention to this symptom.

In surgical diseases of the **spinal cord**, the general symptoms of increased pressure are far less important than those of local origin which give rise to paraplegia. The histological changes which the cord suffers from pressure have been well studied in animals by placing aseptic foreign bodies, laminaria tents, bird shot, etc. extra- and intradurally in the spinal canal (89). Swelling and vacuolization of the cells usually followed, due mostly to lymph congestion. Inflammatory changes were occasionally observed (see Enderlen). It is an open question whether the lymph congestion acts mechanically on the nerve tissue or whether it interferes with nutrition (90).

The effects of concussion of the spinal cord are similar to those of the brain so the reader is referred to that paragraph (36), (82). Experimental investigations have been undertaken by Schmaus and Newton (91). The most important pressure producing conditions in man are tuberculosis of the vertebræ (92) and gun shot wounds. In both cases, inflammatory changes are added to aseptic pressure. This has been investigated experimentally by Israi and Babes, among others, using mustard oil in the spinal canals of dogs. Particularly in caries of the vertebra, the question is often debated of whether the myelitis follows the pressure, or whether it is from the spread of inflammatory processes (93). Such an accentuation of one pathological process should always be avoided in a complicated disease. That both may cause the paralysis in question is shown by our experiences in laminectomy for vertebral caries.

In gun shot wounds also, the mere mechanical influence of a foreign body embedded in the spinal cord should not be considered without recognizing the danger of an infection spreading from it. This question is, of course, important in the decision of removal or non-removal of the bullet in any given case. Braun (94) has carried out experiments to clear these points. He embedded small shot in the spinal cords of dogs and then examined the changes histologically, coming to the conclusion that "the gravity of the lesions depends on the amount of injury done to the cord while the shot is being embedded, and on the amount of space encroached upon by the shot." The histological changes (89), (95) which follow injuries are manifested in two hours by swelling of the axis cylinders which rapidly spreads and increases in amount. Later, proliferative changes begin. This swelling and cell edema gradually diminish, and thus is explained the early spread and later improvement of the paralyses. An experiment by Braun shows, however, that these injuries which bring about paralyses are caused in part by the presence of the foreign body *per se*. In one of his dogs, in which he had produced severe paralyses by placing a shot in the spinal cord, he brought about an improvement by its removal. This agrees in general with war experiences, and early removal of the bullet seems best, because the danger of secondary infection is always present (96).

The effects of section of the cord on the general metabolism have been reported by Hari (97). Section at the neck is followed by diminished oxygen consumption and blood pressure, while section through the dorsal and lumbar regions has no observable influence. The diminution of gas exchange and the blood pressure run parallel, so that both are probably related to a certain degree to each other. The decreased gas exchange may follow the slowing of the circulation.

The clinical result of such compression or injury is spastic paralysis. Normally, the sensory stimuli coming from the periphery are weakened by inhibitory impulses flowing in the pyramidal tracts from the brain. If these latter fibres are injured or destroyed by pressure, "the 'tension' of the gray matter of the spinal cord, by receiving the unweakened sensory stimuli is increased, and there is a lowered threshold of response" (98). These processes are, of course, not understood in their entirety, but of this much, we are certain, that spasms do not arise in an extremity when all its sensory fibres are cut, or they are diminished in degree if their irritability is lowered. This has been shown in the results of the Forster operation, that is, resection of posterior sensory roots of the cord in spastic paralyses. Such paralyses appear, of course, not only after pressure on the spinal cord, but also in all sorts of brain affections, provided that the inhibitory fibres in the pyramidal tracts are involved. Stoffel (99), in

his operation, attacks the other side of the reflex arc, namely the motor parts, by cutting twigs of the motor nerves close to their insertion in the muscle. In this way, the nervous control is also weakened.

Diseases of the *vertebral column* itself are no different in principal from diseases of the extremities. The influences on the organism of the much used therapeutic measure of suspension by the head may be briefly mentioned. Experiments covering this question were done by Anders and Joachimsthal (100), etc. Anders attempted to discover how the increase in length of the spinal column is brought about, while Motschutkowsky (cited by Joachimsthal) studied its influence on the spinal cord. Certain changes in the position and tension of the roots and meninges were recorded, but they do not seem to have any particular meaning. The same may be said of its influence on circulation, as brought out by Joachimsthal.

#### LITERATURE TO BRAIN AND SPINAL CORD

1. Lit. see Bergmann: Kronlein, Kuttner in Handbuch d. prakt. Chirurgie, 4th edit., 1913, V. 1. Kocher: in Nothnagel's spez. Path. and Therapie, V. 9, 3. Hauptmann: in Neue Deutsch. Chir., V. 11 and 12.
2. Reichardt: Deutsch. Ztschrft. f. Nervheilkunde, 1905, 28; Ztschrft. f. d. ges. Neurol. and Psych., 1911, 3; Ztschrft. f. Psych., V. 75.
3. Naunyn-Schreibeo-Falkenheim: Arch. f. exp. Path. and Phar., V. 14 and 22. v. Bergmann: 1 and Deutsch. Chir., V. 30; Archiv. f. klin. Chir., 1885, 32 v. Volkmann's Sammlung klin. Vortrage, 1881, No. 190. Cushing: Grenzgebiet., V. 9 and 18. Geigel: Virch. Archiv., V. 119, 123, 174, "Die Mechanik der Blutversorgung des Gehirns," Stuttgart, 1890. Hill: Phys. and Path. of cerebral circulation, London, 1896.
4. Adamkiewicz: Wiener med. Wchscrft., 1888; Sitzungsber d. akad.; Wien, 1883 and 1890; Wiener klin. Wchscrft., 1897.
5. Sauerbruch: Grenzgebiet, 1907, 3 Suppl. Breslauer: Grenzgebiet, V. 30.
6. Hauptman: Neue Deutsch Chir., V. 12, p. 208.
7. Mestrezet: Liq. cephal. rachidien, normal and path. Paris, 1912.
8. Lit. see Holzmann: Neue Deutsch Chir., V. 12, 2, p. 204.
9. Lewandowsky: Ztschrft. f. klin. Med., 1900, 40. Quincke: Deutsch. Klinik, 1902, 6.
10. Bungart: Festschrift d. Kolner Akad., 1915, p. 707.
11. Wilms: Not demonstrated in one case.
12. Nonne Apelt: Arch. f. Psych., 1907, 43.
13. Neu and Hermann: Monatschrft. f. Psych., 1905, 124.
14. Hill and Ziegler: Deutsch Ztschrft. f. Chir., V. 65.
15. Schmorl: Zentralbl. f. Pathol., 1910.
16. Klose and Vogt: Grenzgebiet, V. 19. Quincke: Deutsch. med. Wchscrft., 1905. Deutsche Klink. am. Anfang des 20 Jahrhunderts.
17. Propping: Munch. med. Wchscrft., 1909.
18. Reichmann: Ztschrft. f. d. ges. Psychol. and Neurol, 1912. Haller: Grenzgebiet, 30.

19. Grashey: Exp. beitr. z. Blutzirkulation i.d. Schadel-Ruckgradshohle: Festschrft. f. Buchner-Munchen, 1892. Propping: Grenzgebiet, V. 19.
20. Kronig-Gauss: Munch med. Wchschrft., 1902.
21. Linser: Bruns Beitr., V. 28. Rohrbach: Brun's Beit., V. 17.
22. Burrow: "On disorders of the cerebral circ," London, 1846.
23. Leyden: Virch. Archiv., V. 37.
24. Bergmann and Bastgen: Ver. der. phys. med. gesell. in Wurzburg, V. 15.
25. Albert and Schnitzler: Intern klin. Rundschau, Wien, 1894.
26. see Payr: Arch. f. klin. Chir., V. 87, No. 4.
27. Finkelnburg: Deutsch. Arch. f. klin. Med., V. 80.
28. Deucher: Deutsch. Ztschr. f. Chir., V. 35.
29. Nonne: Neue Deutsch. Chir., 1912, 2.
30. Hoessly: Mitt. a.d. Grenzgebiet, 1918, V. 30.
31. Breslauer: Grenzgebiet, V. 29.
32. Ray and Sherrington: Journ. of Physiol., 1890.
33. Begrer: "Zur Lehre von der Blutzirkulation in der Schadelhole," Habilitationsschrft. Jena.
34. Wilbrand and Sanger: "Neurologie des Auges," V. 14.
35. Kocher: Nothnagel's Handbuch d. spez. Path. and Therap., V. 9, 3.
36. Messerer: Exp. Untersuch. uber Schadelbruche Munchen, 1844. Tillman: Arch. f. klin. Chir., V. 57, 59, 66. cited by Hauptman: Gama—alquie—Felizet, Neue Deutsch. Chir., V. 11 and 12. Herrmann: Dissert. Dorpat, 1881. Fisher v. Volkmann's Vortrage, No. 27. V. Brunn: Die chirurgischen Krankheiten und Verletzungen d. Gehirns Tubingen, 1854. V. Bergmann: Deutsche. Chir., 30, and Handbuch d. prakt. Chir., V. 1.
37. Bohl: Deutsch. Ztschrft. f. Chir., V. 43, lit.
38. Teevan: Handbuch d. prakt. Chir., 4th edit., V. 1, p. 65.
39. Tillmann: In Wilms-Wullstein, Lehrbuch d. Chir., 6th Edit., V. 1, p. 69.
40. Collier and v. Schjerning: Ueber. d. Wirkung u. Bedeutung d. neuen Handfeuerwaffens Medizinalabt. d. preuss. Kriegsminist., 1894.
41. Krohnlein: Chirurgenkongress, 1899; Brun's Beit., 1900, 29.
42. Merten: Bruns Beit., V. 108, p. 371.
43. Franz: Bruns Beit., V. 116, p. 443; Arch. f. klin. Chir., V. 93.
44. Doepfuere: Deutsch. Ztschrft. f. Chir., 1912, 116, 44.
45. v. Wahl: Zentralbl. f. Chir., 1888.
46. Pirogoff: Grundzuge d. Kriegschirur., p. 74-75. Stromeyer: Handbuch d. Chir. Beck: "Die Schadelverletzungen," Freiburg, 1865. Kramer: Ann. of Surg., 1896. Koch and Filehne: Arch. f. Klin. Chir., V. 17.
47. Sauerbruch: Monatschrft. f. Psych., V. 26; Ergänzungsheft, Grenzgebiet, V. 9 and 18.
48. Dreyfuss: Ztschrft. f. d. ges. Neurol. and Psych., V. 7. Friedmann: Deutsch. med. Wchschrft., 1891; Munch. med. Wchschrft., 1893; Arch. f. Psych., V. 23.
49. Friedlander: Virch. Archiv., V. 88. Holder: Path. anat. d. Gehirnschuttering pub., Von Weise, Stuttgart, 1904. Hauser: Deutsch. Arch. f. Klin. Med., V. 65. Tillmann: Arch. f. Klin. Chir., V. 59, 64, 66. Virchow: Virchows Arch. V. 50.
50. Bollinger: Festschrft. f. Virchow, 1891, V. 2.
51. Meyer, A. W.: Mitt. a. d. Grenzgebiet, V. 23.
52. Friedrich: Deutsch. Ztschrft. f. Chir., V. 85.
53. Cassirer: Oppenheim and Cassirer in Nothnagels Handbuch. d. spez. Path., Vienna, 1909, Der Hirnabscess.



54. see Boschard, *Neue Deutsche. Chir.*, 18, 3.
55. Blevgad: *Munch. med. Wchschrft.*, 1915, p. 1065. *Schrfone: Deutsch. Ztschrft. f. Chir.*, 1904, 75.
56. Schrottenbach: *Studien uber den Hirnprolaps in Monographs a.d. Gesamtgebiete d. Neurologie, etc.* Springer, 1917.
57. Oppenheim: *Lehrbuch d. Nervenkrankheiten*, 5th Edit., 1908, p. 1087. *Deutsch. Ztschrft. f. Nervenheilkunde*, 1897 and 1907. Quincke: *V. Volkmann's Sammlung klin. Vortrage*, 1893. No. 67. Wendel: *Arch. f. Klin. Chir.*, V. 99. Boenninghaus: "Die Meningitis serosa," Wiesbaden, 1897.
58. Axhausen: *Berlin klin. Wchschrft.*, 1909.
59. see Bircher: "Schadelverletzungen durch mittelalterliche Nahkampfwaffen," *Arch. f. Klin. Chir.*, V. 85.
60. Hartmann and di Gasparo Lewandowsky: *Handbuch d. Neurologie*, V. 5. Braun: "Epilepsie nach Kopferletzungen" *Neue Deutsch. Chir.*, 18, 3.
61. Redlich and Binswanger: "Die klinische Stellung der sogenannten Epilepsie, Berlin, 1913, pub. Karger. Redlich: *Deutsch. Ztschrft. f. Nervenheilkunde*, 1909, V. 35. Binswanger: "Die Epilepsie," in *Notlnagel's Handbuch*, Wien, 1899.
62. v. Orzechowski and Meisel: Cited by Bauer; *constitutionelle disposition zu inneren Krankheiten*, Berlin, 1917, Springer.
63. Alzheimer: *Ver. deutscher Nervenarzte*, 1913, 7.
64. Marburg and Ranzi: *Wien. klin. Wchschrft.*, 1917, No. 21.
65. Fritsch and Hitzig: *Arch. f. Anat. u. Physiol.*, 1870.
66. Goltz: *Lit. Ito-Deutsch. Ztschrft. f. Chir.*, V. 52.
67. Westphal: *Berlin-klin. Wchschrft.*, 1871.
68. Adamkiewicz: *Berlin. klin. Wchschrft.*, 1885.
69. Nothnagel: *Virch. Archiv.*, 1868, 44. Tenner: "Moleschotts," *Untersuch. zur Naturlehre*, 1857, 3.
70. Ziehen: *Arch. f. Psych.*, 1890, V. 21.
71. Magnan: *Arch. de physiol.*, 1873, V. 5.
72. Heilbronner: *Handbuch d. inneren. Med.*, V. 5, p. 837.
73. Charrin: *Arch. de physiol.*, 1897, 29.
74. Tilmann and Bungart: *Festschrft. d. Kolnes Akad.*, 1915, p. 733; and *Munch. Med. Wchschrft.*, 1912.
75. Landois: *Deutsch. med. Wchschrft.*, 1887.
76. Voisin and Petit: *Arch. de Neurol.*, Vol. 30.
77. Sauerbruch: *Chirurgencongress*, 1913.
78. Kussmaul and Tenner: *Moleschott's-Untersuchungen zur Naturlehre*, 1857, V. 3. Kellie, 1824: *Piori-Travers-Hall-Mayer*, Cited by Ito, *Deutsche Ztschrft. f. Chir.*, V. 52, lit.
79. Herman and Esches: *Pfluger's Arch.*, 1870, 3.
80. Bier: *Mitt. a. d. Grenzgebiet*, 1901, 7.
81. Momburg: *Deutsch. med. Wchschrft*, 1914. Eastman: *Am. J. Med. Sci.*, 1915.
82. Kocher: *Deutsch. Ztschrft. f. Chir.*, V. 35 and 36.
83. Nowatski and Arndt: *Berl. klin. Wchschrft.*, 1899, No. 30.
84. Friedrich: *Arch. f. klin. Chir.*, V. 77, No. 3. Moeckel: *Dissert. Heidelberg*, 1915.
85. Brodmann: *Neue Deutsche Chir.*, 18.
86. Cited by Thale: *Mitt. a. d. Grenzgebiet*, V. 3.
87. Friedrich: *Deutsche Ztschrft. f. Chir.*, V. 67, p. 656.
88. Wilms: *Mitt. a. d. Grenzgebiet*, 1903, V. 2. Also Clairmont, *ibid*, V. 19.
89. Enderlen: *Deutsche Ztschrft. f. Chir.*, V. 40. Kahler: *Prager. Ztschrft. f. Heilkunde*, 1882. Rosenbach and Schschterbak: *Virch. Arch.*, V. 122.

90. Rumpf: Pfluger's Archiv., V. 26.
91. Newton: Brit. med. J., 1913, p. 1101. Schmaus: Munch. med. Wchschrft., 1899, 1.
92. Babes: Vierteljahrsschrift f. Dermat. u. Syphilis, 1882, V. 9. Schmaus: "Die Kompressionsmyelitis bie Karies," d. Wirbelsaule Habilitationschrift, 1890.
93. Michaud: These de Paris, 1871.
94. Braun: Deutsche Ztschrft. f. Chir., V. 94.
95. Schifferdecker: Virch. Arch., 1876, V. 67.
96. Heineke: Lehrbuch d. Kriegsschr. Borchard Schmieden. Marburg and Ranzi: Arch. f. Klin. Chir., V. 111 and Wiener klin. Wchschrft., 1915. Perthes: Bruns Beitrage, V. 97.
97. Hari: Biochem. Ztschr., 1918, V. 89.
98. Forster: Ergebn. d. Chir., V. 2, p. 176.
99. Stoffel: Vulpius-Stoppel Orthopad-Operationslehre Stuttgart Enke.
100. Anders: Arch. f. Klin. Chir., V. 38, p. 58. Joachimsthal: Arch. f. Klin. Chir., V. 49, p. 460.

## CHAPTER XII

### EXTREMITIES

The framework of the body, particularly of the extremities, is made up of the *bones*, in conjunction with the *joints*, *tendons* and *muscles*.

The shapes of the bones are closely related to their functions, and since these in their turn depend on the action of the muscles, it follows that muscles and bones are mutually interdependent. In all therapeutic measures, therefore, particularly in fractures, we must bear in mind this close relationship. We cannot attain ideal healing of a fractured bone without considering the functions of the muscles involved, and *vice versa*.

The task of bone tissue is to offer resistance to push or pull (1), and the long bones are also subjected to bending stresses. The performance of these functions is the stimulus which preserves their form and structure, and if it is removed or diminished as in paralyzes, atrophy follows from the activities of osteoclasts. In addition, a so-called flat or smooth atrophy has been described by certain authors (Roux (1), p. 228), but we will speak of this disuse atrophy in greater detail a little later.

The finished bone is not built homogeneously, but as is well known, consists of an outer compact layer, and an inner spongy layer. The marrow cavity occupies the center. The hardness, density and elasticity depend in the main on the superficial layer of the compacta, but these three parts vary under physiological and pathological conditions. Young bones are more elastic, in that they contain relatively less inorganic matter (2); the bones of adults, on account of their greater calcium content, are harder and denser, and, therefore, break less easily than those of children, but since the periosteum is stronger in the latter, the so-called green stick fracture is more common, that is, a fracture in which the bone is bent, but the periosteum remains unbroken and prevents displacement of the fragments.

The *form taken by a fracture*, ignoring the influence of the force, is determined by the shape of the bone. Bending breaks are more common in long bones, compression fractures in short bones. The direction taken by the lines are in accordance with the physical laws of pull, push and pressure, and it is possible, as shown in every surgical course, to reproduce a given fracture experimentally on a cadaver, after the action of the forces producing the break have been studied in the patient. In general, longi-

tudinally running lines indicate compression, transverse lines, bending or shearing.

The displacement of the fragments is closely dependent on the musculature, for every muscle in the body is stretched somewhat beyond its natural length and has a definite tension with each position assumed by the joint. For this reason the central end of a tendon quickly retracts after severing, and, in a break of the bony scaffolding, which determines the tension of the muscle, the fragments are pulled toward and over each other, and the displacement occurs in the longitudinal axis. The tension is retained after death, for the muscle retracts when it is severed (3).

This passive stretching allows of a quick approach of its points of attachment at the very beginning of contraction. If the muscle were thoroughly relaxed at the beginning of a movement, a part of its strength "would be lost without producing a mechanical effect" (Luciani). But the traction is not entirely passive, but is influenced by what we call "tonus," that is by a tension which is an expression of the living energy of the muscle (Luciani), and which depends on its nervous innervation.

Accurate measurements of the tension imposed on the bones normally and when weight is applied, are given by Grunewald (4).

*Muscle tonus* is the most important force which holds the bones against each other and keeps the joint surfaces in contact. The latter, of course, are held in their definite positions by the capsule and ligaments, but these means of support are not sufficient to keep them safely in position. In certain situations, shoulders, hips, and fingers, atmospheric pressure, as shown as early as 1836 by E. Weber (6), helps to press the head into the socket and keep it there. Experiments and measurements recording the effect of this factor on the various joints have been made by Aeby (7). But it is certain that muscles play the largest part in the approximation of the surfaces, for if they relax or become paralyzed, a very insecure joint is the result. Abnormal mobility as seen in contortionists, or in rachitic children, depends on a pathological relaxation of the musculature (8), or perhaps on the ability of the particular person to allow the antagonists to become more relaxed during certain movements than is possible in a normal individual. Bing (9) found certain histological changes in the musculature of rachitic children, which he believes is responsible for the abnormal laxness; furthermore, he found a diminution of their electrical irritability.

In functioning, muscles alternately exert pressure and pull and these forces are functional stimulants to the bones and may lead to changes in their structure. This *internal remodeling* shows itself particularly in the spongy trabeculæ, and is one of the best and earliest known functional adaptations in the body (10). If the bone is used vigorously, it hypertro-



phies, and a change in its internal structure occurs "trajectorially." It may also increase in size locally, under increased demand for function as, for example, the thickening of the cortex on the concave side in bowing of the legs (Roux, p. 226). These changes in the form, etc., do not occur as R. Fick (11) believed, from "plasticity," as in a piece of clay, but according to "a regulated reaction of the bone and cartilage in response to different mechanical stimuli," which Roux (1) calls "the functional adaptation." There is no necessity of discussing the question which has played such a large role in surgical literature, of whether the largest number of cases of pathological bowing can be better explained by pressure, or by a response to functional demand. The impression is gained from reading the different works, that the arguments were really far fetched (12). In their more general relations, all these deformities follow the ordinary laws of statics and mechanics just as the normal movements of the joints. Details of this may be found particularly in the assembled work of R. Fick and Strasser (13).

The above remarks (14), that readjustment of the skeleton may occur in adults through action of muscles, brings up the question of whether the growth of the skeleton is related to the muscle anlagen in embryonal life also. This does not seem to be the case in a certain lower animal according to the investigations of Braus (15), who found rather a wide independence in the development of the skeleton and the musculature ("self-differentiation").

That the form of muscle also depends on the skeleton has been shown experimentally by a number of workers who started with the known observation, that negroes, even when very muscular, usually have a small calf in comparison with Europeans (16). The development of the calf muscles is closely associated with the length of the tuberosity of the os calcis; if this is long, the tendon of Achilles is short, and the calf muscles are more prominent (as in Europeans). If the tuberosity is short, the Achilles tendon is very long and the muscles of the calf are confined to a small localized prominence a short distance below the popliteal space, while the remainder of the calf shows no bulging (as in negroes). Marey and Joachimsthal produced a definite change in the calf musculature of animals by shortening the tuberosity of the os calcis; an alteration in length of muscle and tendon which is obviously an adjustment to changed function. It follows from this, that a smaller circumference of a joint does not necessarily point to a less important function.

Now a muscle which grossly seems of uniform structure does not have a uniform function throughout. Modern physiology, (see Luciani), takes the standpoint that in every striated muscle there run two kinds of fibres, the red, rich in sarkoplasm and the white, rich in fibrils. The red fibres are

said to contract more slowly, and, as Grutzner, puts it, are an "internal brake," that is, they prevent a rapid relaxation after contraction. In lower animals, this differentiation of function often lies in different muscles (17). Thus, according to v. Uxkull (18) the spine of the Echinoidea (Sea Urchin) has an outer movement muscle and an inner "brake" muscle. The latter functions so that "with every change of body weight, either in the direction of increase or decrease, changes in the tension are equalized." To preserve the proper degree of tension, this function is regulated by impulses from the centers. In mechanics, there is nothing to compare with this exquisitely regulated mechanism. The muscles are not as a rubber band which stretches a certain amount with a small weight, and correspondingly more with a heavier weight, but there is a definite threshold and nothing occurs until this is passed, after which there is maximum contraction. These remarks, of v. Uxkull, apply in a general way to the muscles of the human, even if there is no actual separation of the two muscle groups.

In man, the knowledge of this double function was first gleaned from the anatomical studies of Boekes (19), who found in each fiber both medullated and non-medullated nerves, which ended among the fibres in different ways. By careful dissection, he separated quite clearly these two kinds of nerve filaments. Physiological and clinical investigations (20) based on these studies, differentiated the rapid muscle twitchings from the more leisurely muscle tonus, as Mosso (21) had already done, but contraction and tonus are so intimately connected in all muscular movements as well as in their function of support, that it seems unprofitable to differentiate them for clinical surgical purposes, except in certain particular questions. Thus, for example, the muscle cushions of amputated arms robbed of their natural insertion, lose more or less of their tonus.

For practical purposes still another division has been established (22). If a peripheral stimulus such as an injury reaches a muscle it reacts in different ways, according to whether it carries a load or not. If it carries a load, as for example, the biceps with a fixed elbow joint, it becomes hard (tonus function) without changing its length. If it is unloaded when the stimulus is applied (biceps with a movable elbow joint), it shortens without becoming hard. This point of view has considerable significance in the management of fractures. The injury which occurs to the muscle at the time of fracture, and the damage after the injury, such as compression between the broken ends is very irritating to it. The ends of the fragments are pulled over each other with greater force than if only the normal tonus were operating, and the muscle stubbornly resists every effort at separation by contracting and remaining in a state of board-like rigidity. Efforts to overcome this resistance with sudden force lead to

severe damage. In the first few hours after injury, the muscle is said to be in a state of shock, according to Zuppinger-Christen (23), so that it does not react to these different injuries, but this idea is not generally accepted (Matti (2)).

We have, until now, spoken only of the function of muscles in connection with their likeness to an elastic band, and their activities in holding the skeleton firmly together. They have a second function, *viz.*, the service of locomotion by shortening and elongating. In every such complicated movement, and these are seemingly the least complicated in our body, a whole group of muscles and not a single one acts, so that, as Du Bois-Reymond (24), points out, the morphological grouping of muscles, as taught in anatomy, gives an entirely false picture of their functional performance. Even the more recent classification into certain systems regards an action occurring in a limited time as a "special case," for, if the movement occurs toward one or another direction, entirely different groups are called into action in each case. Thus, there is a continuous change in the grouping, and there are "antagonists" and "synergists" only at the time of movement, and not in the permanent sense taught by anatomy. This is further complicated by the fact that a number of muscles pass over two joints, and contribute to the movements of both.

The influence of a muscle, however, reaches still further. As pointed out particularly by Otto Fischer (25), it does not, in the main, seek to move only one joint, but to bring a whole part of the body into motion, and it follows that the muscle finally acts not only on those joints and bones over which it plays, but also on joints which are apparently entirely out of its sphere of action. This has important practical bearing. We will see in discussing muscle and bone atrophy, how this distant influence makes itself felt. The same holds true in deformities.

This influence is exerted not only when they actually contract, but also when they enter a state of tonus, and like a transmission belt, bring about movements. This coordinated movement of muscles may be illustrated when the knee is forced to bend and the heel to rise by the flexing of the hip joint (26).

The variety of movements which muscles covering several joints are able to bring about, makes it necessary that they slide over the bones underlying them, but only when the joints involved are moved in a particular way. During the opposite movement, the muscle remains quiescent. This fact is used in therapeutic measures, as for example, the fragments of a fractured patella are brought as closely together as possible by strong flexion of the hip with the leg extended at the knee. Furthermore, it explains why the adherence of a muscle to a fracture leads to such disturbances of motion.



Since the amount to which a muscle can shorten is limited, and since according to Schwann's law this power diminishes rapidly as its length decreases, it follows when a muscle covers several joints, that the movement of one joint is incomplete when the other joint is also moved, because the strength of the more than one jointed muscle fails. For this reason, we cannot easily extend the knee in a sitting posture, or close the hand freely with the wrist maximally flexed, nor open the hand with the wrist fully extended. This is spoken of as the "relative insufficient length of muscles crossing two joints" (27).

In every joint, or rather in each of the extremities as a whole, there is a position in which all the *muscles are in equilibrium*, i.e., no muscle is particularly stretched or particularly relaxed, and there is definite rest for the limb. In the leg, this is when the knee and hip are bent and the ankle in such a position that the foot points slightly downward. These rest positions have secured full recognition in the modern treatment of fractures. If we apply a stretching bandage to a leg in this rest position, we need much fewer weights to correct the shortening than if the knee and hip are extended and the foot is in a right angled position, that is, all the muscles are evenly relaxed and the pull which is necessary to compensate for a longitudinal displacement, according to the above remarks, meets the least resistance. This lighter weight, of course, produces a smaller injury to the muscles. As a consequence, the functional results in fractures treated in a semi-flexed position are considerably better than those treated in full extension. That the much used position of extended knee, almost extended hip, foot in a right angled position, is unphysiological, can be demonstrated at any time on one's own body by the feeling of stretching and fatigue. No person without compulsion would assume this position asleep in bed.

These rest positions are equally important in the arm, as in a typical fracture of the radius or humerus. If an arm broken into the diaphysis is bound in a triangular splint, there will result a dislocation to the periphery, and after healing, the patient holds the hand so that the back of the hand instead of the thumb, is anterior. Therefore, when the humerus is directed away from the body at an angle of  $45^\circ$ , it is necessary to bring the forearm parallel to the ground.

The injury which occurs even with passive stretching, is effective also in a paralyzed muscle. The muscle loses its elasticity and tonus (28). Therefore, the rule in paralysis of the radial nerve, not to allow the hand to hang, but to keep it on a splint in a mid position, otherwise the extensors will be so damaged that their function will not return completely, even when innervation is reestablished.

By *muscle sense*, we understand with Sherrington, the total sensory



impulses which originate in the motor apparatus, namely, muscles, tendons and ligaments. That muscles are sensitive to pain is seen in goiter operations during which the muscles are divided and sutured. Probably the pain sense is related to the nerves which accompany blood vessels, at least, the sensitivity of the muscles is still preserved, even increased when the plexus supplying the arm is completely paralyzed (29). In stretching, the muscle is also sensitive to pain.

Furthermore, a muscle has a pronounced *sense of position*, although it is questionable whether we are aware of the position occupied by a certain joint by means of this "deep sensitivity," or through sensory paths from tendons, joint capsules, and ligaments. Modern physiology and neuropathology have taken a stand on this question (lit. see Luciani (3)). It may be said that there is a relation between skin sensitivity and deep sensation, but in spite of disturbances in the former, there is a definite appreciation of the position of the parts of our body from deep sensations (30). Particularly instructive and consistent are the experiences of surgeons, not only with local anesthesia, but also in injuries to single nerves. We know that a finger that has been made insensible by a local anesthetic injected at its attachment to the hand, does not know its position in space, even though the muscles and higher located tendons are undisturbed in their innervation. Similar observations have been made in injuries of single nerves in the arm or leg. More exact experiments have been made by Lehmann (31). He could find changes in position sense and movement disturbances only through injury of the tibial, ulnar and median nerves. In his experiments, for instance, it was easy to separate skin sensitivity from position sensitivity of the thumb, by paralysis of the median nerve. The skin of the thumb is, of course, partly supplied by the radial nerve. In lower animals, the independence of skin sensation and deep sensation is shown best by Claude Bernard's experiments, in which he removed the skin of a frog and found no changes in its ability to move.

In regard to the second question of whether deep sensation is transmitted from muscles, or from joints and ligaments, physiologists believe in general, that the sensitivity of ligaments is more important than that of muscles, particularly because of the consideration that the latter, especially when they cover several joints, have such varied functions. It is, therefore, not very probable that the sensations of definite position in a joint are transmitted from the muscles alone, although from the standpoint of the surgeon, the position sense of a muscle must not be underestimated. At least, in amputations and disarticulations, there is a greater surety of movement and better knowledge of the momentary position of the operated member, if the muscle parts or tendons are sutured over the stump. Furthermore, the experiences with artificial joint mobilizations have shown

that the patient with closed eyes, can tell exactly what position his joint occupies, even if all the capsule and ligaments have been removed (32).

The whole subject of position sense is made still more difficult by the fact that central sensations arise, which precede an actual movement. A number of the most prominent physiologists and psychologists such as Johannes Muller, Helmholtz, Wundt (33) and others are of the opinion that we not only feel the movements which are carried out, but also intended movements. But this theory of central innervation which can only be mentioned here, does not receive general recognition (see Luciani (3)). How the final regulation, and switching about, or shunting of muscle function and its sensation are controlled in the centers, is shown among other ways by the surgical observations in the *learning of a new function* in muscle transplantations. This "learning anew" occurs consciously at first. When, for example, as in one of E. Schmidt's published cases, the latissimus dorsi was transplanted on the biceps, the patient at first could bend his arm only if he consciously prepared himself to reach backward. Later the bending was done without such a preparation. The same occurs in the building of muscle channels according to the method of Vanghetti-Sauerbruch (34). Of course, the conditions are not so complicated in this case, since, whenever possible, flexing muscles are employed to flex, and *vice versa*. If this is not done, but flexors are united to extensors, the weakness of the extensors in comparison to the flexors is at once apparent, since, by this artificial arrangement, they must learn this function gradually (34).

A similar lesson must be learned in paralyses when a movement is taken over by other muscles. It may happen that a small part of a muscle will attempt to perform a new function, while the larger part goes on quietly with its old function. Thus Kron (35) could so teach the pectoralis major that its clavicular portion replaced the paralyzed deltoid.

Finally, it must be recalled in this connection that certain individuals who have had a limb amputated, still have the sensation as though the member were present, and think they can move the toes of the amputated foot.

If a limb is partly paralyzed or if its movements are hindered by stiffness or partial ankylosis, every movement demands an increase of innervation force, and patients are exhausted after small efforts, even if the work performed is trifling compared with that needed to tire a normal muscle. All this leads to the conclusion that the theory of central innervation has much in its favor.

If a muscle loses its point of insertion it not only fails to keep pace with the general body growth, but also atrophies. This is the reason stumps of amputations done during childhood become conical in shape (36).

That such a highly differentiated structure and one whose function is so nicely adjusted to the place in which it lies, should withstand *transplantation* poorly in spite of ability to learn new tasks is quite obvious. The possibilities of transplantation have been studied in both animals and man (37). Eden, who has recently reviewed the literature, reaches the conclusion "that, as yet, there has been no proved successful case of free muscle transplantation." The transplanted muscle heals, but in a short time it is replaced by connective tissue. The difficulty of all these procedures is that muscles, blood vessels and nerves, are all an inseparable unity, and an interruption of the blood supply for even a short duration is tolerated very poorly, and, as we will see, without its nerve supply, the function is entirely lost.

The question of whether wounds and defects are filled in by connective tissue, or whether there is a *power of regeneration*, is answered in a different way by the clinician than by those who base their conclusions on animal experiments. Zenker (38) had pointed out that a widespread regeneration must take place following the necrosis of muscle during typhoid fever, since at later autopsy no fibrous scars are found, but, on the contrary, muscle tissue capable of functioning. Kuttner and Landois (39) also take the viewpoint, that, in time, human striated muscle regenerates much more widely than seems to be indicated by animal experiments. They also point out that a complete regeneration of striped muscle tissue may be observed in old completely healed fractures which may be studied at a later autopsy. Finally, Bier (40) insists that, in man, even large muscle defects may be filled in by functioning muscle tissue, and almost the whole of the pectoralis major may be rebuilt after amputation of the breast. In contradistinction to these experiences in man, there are found in animals only slight beginnings of regeneration, with single muscle buds, when an injury with loss of substance is produced (41). The difference may be explained by the probability that muscle regeneration requires a much longer time for completion than has been allowed in animals, but if, and how, functional muscle tissue arises in muscle scars cannot be found in the cited works.

*Healing of a fractured bone* occurs by the growth of the so-called callous, the details of which can be found in text books of pathological anatomy. A point of argument which is not completely settled, concerns the part played by the bone marrow in the formation of callous. From the pathological anatomical viewpoint, the significance of marrow callous was held to be small, but surgeons were always of the opinion that the marrow takes a prominent part in the healing of a fracture, particularly after their experiences with operations for pseudo-joints (42). To make a pseudoarthrosis heal, it is necessary to freshen up the ends of the bones until healthy



marrow appears. Many procedures which are followed by particularly successful healing of pseudarthroses have carried out this exposure of healthy marrow unintentionally. Recently, Martin has shown experimentally, that the formation of new bone depends on the work of marrow, cortex and periosteum. Transplantation of periosteum is successful only if some of the superficial layer of bone is carried along (43). This agrees very well with the experience in resection of ribs, where the bone is incompletely rebuilt after subperiosteal removal. Bier also emphasizes this statement on evidence from his experimental investigations. When the circulation is disturbed in a bone, fractures will heal poorly (44), but division of the nerves is without influence, as experiments and numerous clinical experiences, especially during the war, have shown (45).

The *pain sensations of bone* have been studied by many, and the experiments of Nystrom are especially valuable because they were done very carefully on himself (46). As is well known, he found the periosteum so richly supplied with sensory nerves that exceptionally severe pain was felt even on simply touching the part or slightly stroking it. The pain was different from that experienced when the skin was cut; it was more diffuse and "blunt," as Nystrom calls it. The cortex separated from its periosteum is completely insensitive; the compacta is similarly so to a depth of several millimeters. The marrow cavity is not insensitive throughout, as Nystrom in contradiction to earlier investigations, has shown beyond criticism. He speaks of a diffuse dull ache. Probably the nerves are present only sparsely, since needle pricks elicited pain only here and there, and Nystrom believes they lie on the inner side of the corticalis. The spongiosa is also supplied by pain nerves, but equally as sparsely. That the bone marrow in rabbits is very sensitive has been shown in studies on osteomyelitis. But the nerves are not distributed uniformly in the skeleton, at least the statement is made (47) that short and flat bones are less sensitive than long bones. Joint and epiphyseal cartilages are insensitive, and the pain in dislocations of joint cartilages is to be explained by pressure on the bones (joint mice) (48).

If an extremity is placed at rest, or spared for any reason, not only do the *muscles atrophy*, but as the investigations of Sudeck (49) have shown, the bones also (39). In the leg, the quadriceps is especially affected, while the flexors remain intact for a longer period, and in resections of the knee joint, for example, there is a later contracture of the flexors. A muscle, the seat of such a simple atrophy, shows a diminution of its electrical irritability without reactions of degeneration. Such cases are generally spoken of as disuse atrophy implying that the muscle deteriorates through nonuse. Atrophy may, however, occur so rapidly in acute inflammations



or after injury to joints, that one is inclined to think of some special pathological physiological process to account for it. There are also many other considerations against regarding this process as arising merely from disuse.

It will help in an understanding of the question if we first consider our knowledge regarding *increase in muscle mass* under normal conditions. The widely held belief that the laborer has a stronger arm than the man who works with his brain is entirely erroneous. The mass of muscle is influenced much more by the original muscle anlagen, as Grunewald (50) among others has stated, and increase in size through exercise occurs only when the muscle performs particularly hard work by lifting a heavy weight in a given time. An increase in musculature presupposes an increased load over short time intervals. If a muscle works against an ordinary load over a longer time, for example, in long distance swimming, running, etc., no increase in size takes place (51); and furthermore, a musculature made especially massive by manipulation or exercise becomes weaker when the individual ceases these exercises even if he performs ordinary physical labor the whole day. We see this very often in those unfortunate patients whose muscles, enlarged by orthopedic procedures, decrease again, when the patient resumes his regular work, even if it is rather heavy. Strength muscle is, therefore, to be differentiated from endurance muscle. The effect on the musculature of more work in a time unit, must not be confused with the results of more work in endurance, as was done, among others, by Horvart (52), and Grunewald (50).

Work hypertrophy of muscles in adults does not follow simply because of better blood supply or nutrition, but is always an adaptation to greater loads. Simple laws of mechanics are basic for hypertrophy, and the only difference in the work capacity of a muscle and a steam engine lies in the inability of the latter to enlarge independently, and to compensate for increased demand by proportionate enlargement of its piston diameters, an ability which the muscle has by virtue of increase in its mass.

The statement that at times a muscle will atrophy following too great a demand for work, as for example, the muscles of the thumb in a file cutter, must be accepted with caution (54). Furnrohr could show in his cases, that the seeming overwork atrophy was really a progressive muscular dystrophy, and the work was a secondary factor (55). In general, we know that an overstretched muscle also atrophies (56).

The question now arises if a healthy man can bring a muscle to atrophy through sparing it. As far as it concerns a muscle hypertrophied by previous exercise, the question has been answered above in the affirmative. Endurance muscles retain their circumference stubbornly, so that a general muscular atrophy is said to be a certain indication of some pathological

process in the affected limb. But this is to be taken with a grain of salt, because experiments have shown that atrophy of the musculature and bone will take place in healthy animals after a limb is kept in complete rest; a finding which certainly agrees entirely with clinical experience (57). Particularly enlightening are the anatomical investigations of Sulzer. Partial rest also will lead to atrophy of muscles and bones in animals. Schiff and Zack, Brandes, and Krauss (58) and many others, observed, after severing the tendon of Achilles in rabbits, that an atrophy occurred, involving not only the gastrocnemius, but also the other muscles of the leg and the os calcis. This fits in with the previous remarks regarding the influence of several jointed muscles on distant parts of a limb (O. Fischer). Further, Grossmann obtained an atrophy of those muscles of the larynx supplied by the inferior laryngeal nerve after section of the superior laryngeal; but these experiments are certainly much confused, and it seems deceptive to speak of a partial rest position in this case. For, as must be repeatedly emphasized, the work which must be done by a muscle to retain the equilibrium, and thus keep an extremity in its normal position (internal work), is considerably greater on the whole than that required to casually change the rest position (for example, flexing the arm), (external work) (59). When the internal work of a muscle is taken from it by removal of the activity of its antagonists, it is injured in its function (in case it has no other antagonists), to an amount corresponding to not only partial but complete immobilization. On such a complete abolition of even the smaller movements is founded the superiority of all really fixative bandages in the treatment of inflammations, which Heidenhain (60) has recently brought again to attention from some observations on himself.

A seeming separate type among the causes of muscle atrophy is disease of joints. In this case, atrophy is said to occur in an exceptionally short time, in fact, without a previous complete inactivity of the muscles (61). A number of authors therefore assign the reason to direct extension of the pathological process from joint to muscle or to nerve endings, a conception which was not borne out pathologically anatomically, entirely apart from the fact that the atrophy of muscle groups distant from the diseased joint would not be sufficiently explained by this reasoning (62).

The widest acceptance has been won by the reflex theory as proposed by Brown-Sequard (63). Raymond, Deroche, and Hoffa sectioned the posterior roots of one side of the lower dorsal and upper sacral cord in animals, and produced an inflammation of both knee joints by injections of irritant chemical substances such as turpentine or silver nitrate. Muscle atrophy occurred only on the side in which the nerve roots were intact. Therefore, a break in the sensory reflex arc protects from atrophy

and this demonstration seems to prove Vulpian's reflex theory that stimuli from inflammatory joints pass from the sensory arc to the motor cells of the anterior columns and damage the trophic centres of the muscles belonging to them. At the autopsy of a patient with muscle atrophy of one leg, Klippel (64) found a diminution in the number of ganglion cells in the spinal cord on the diseased side, but Duplay and Vazin (65) in experimental joint inflammations found no such change.

This reflex theory was immediately combated, and Sulzer (57), for instance, insisted that in the experiments of Reymond-Deroche, the atrophy following section of the roots in the sensationless leg was not so outspoken because the leg in question was not spared as the other one, on account of lack of pain. Schiff and Zack (57) carried out experiments in opposition to the reflex theory in the following way. They sectioned the dorsal spinal cord transversely, which left the reflex arc intact. Following this, they observed a rapidly progressing disuse atrophy of both legs. When they injected turpentine into the knee joints of animals so prepared, they found the musculature remained stronger in the injected leg than in the other, while according to the reflex theory, the reverse should have occurred. Schiff and Zack explain this curious finding by assuming that there is a constant irritation from the arthritis acting reflexly on the musculature. The conditions are said to be exactly opposite to those expected according to the Vulpian theory.

At any rate, these experimental results show once more that in the last analysis a muscle remains normal because of continuous nervous impulses, which produce what we call tonus; and in truth, it seems from clinical experience that these impulses are enabled to produce their optimum effect when the musculature is in a mid-state, *i.e.*, when there is equal muscular tension between flexors and extensors, adductors and abductors, etc.

Further, von Tilmann (56) and Kremer (56) have called attention to the possibility that atrophy in all sorts of diseases of the extremities can be produced by overstretching. Each muscle, of course, has a certain elasticity which has been measured fairly accurately by physiologists (66). It is known from the work of Mosso (67) and others, that a muscle which has been stretched from its resting position retracts somewhat after the weight is removed, but it never returns to its original length. This Tilmann could confirm, and it is very easy to believe that a muscle can be damaged by prevention of its return to a normal resting position over a certain length of time. Thus an atrophy of individual leg muscles can be due to overstretching from partial or complete flat foot. Such an unphysiological overstretching takes place when the leg is placed on a Volkmann's splint with the hip and knee extended, and the foot flexed



at a right angle; a position in which we must keep the limb in joint inflammations for other reasons which need not be discussed here.

Roux (1) showed that an atrophy following disuse occurs only in those dimensions which "functioned more weakly." If we, therefore, prevent extension and flexion of a joint, atrophy occurs only in the length of the muscles belonging to it. The same considerations apply to bone atrophy in which the degree and rapidity can be followed by x-ray studies (68). It also progresses with extraordinary rapidity, and in animal work, clear cut changes can be noticed in two to three weeks after placing a limb in a plaster cast. The histological changes in bone atrophy have been recorded by Roux (1).

In children—less clearly in adults—a well marked disturbance of growth of the affected limb also occurs (69). This is not because of injury to the epiphysis as Konig (70) believed, since bones in which the epiphysis is not affected at all are also retarded in their growth. Wolff showed by accurate measurements, that it is only the foot which is backward in its growth, no matter what the disease of the leg (infection of knee joint, etc.), and he is, therefore, of the opinion, as is Sudeck also (68), that the nervous system is involved.

The above mentioned remarks against the Vulpian reflex theory in its original form apply, of course, to *bone atrophy*. But the fact must also be explained that not only do those bones and muscles atrophy which are themselves placed at rest, but others also which seemingly are not at rest. It was stated above that the muscles are not to be regarded as single objects but as groups, and in truth, modern descriptive anatomy teaches that many, even distant muscles, belong to such "kinetic chains." It seems comprehensible that when one link of the chain is injured the others will suffer in more or less degree, since their stimuli are then sent through different paths. That bone atrophy is related to muscle atrophy and is dependent on it, cannot be shown in all cases, but it is not improbable that the relation is there nevertheless.

Disturbances in the normal stimulation lead, therefore, to atrophy, and, to repeat, the impulses which are followed by "external" work of the muscle (for example, flexing the arm) are not the only ones of importance, but the continuous ones which determine the "internal" work (the position of the joint) are of equal if not greater significance. The true value of these little movements in surgical treatment, particularly in the management of fractures, was first recognized by Bardenheuer (71) who placed particular emphasis on the necessity of patients innervating their own muscles to avoid atrophy while on an extension apparatus, while the opposite was practiced by Lucas Champoniere who treated fractures in utmost extension from the beginning, that is, he valued the "external"



work of the muscles and passive movements of the joints more highly. But the superiority of active innervation to all passive manipulations for the health of the muscles, is now fairly well established.

The theory of Grunewald (50) that the atrophy depends on a lack of hormones as in the process of involution of the uterus, lacks sufficient evidence.

The *atrophy of muscles following section of the nerves* supplying them has been studied particularly by neurologists (72). Jamin's work on animals showed that there is a diminution of the primitive striæ with disappearance of the cross striations in a short time, and finally, gradual complete disintegration of the muscle fibres (73). In general, it is said that this progressive degeneration causes the muscles to lose their faradic irritability in 12 days; a statement which must be modified by the findings of Vulpian and Perthes (74). The latter showed in operations on gunshot wounds of the nerves, that the naked muscle retains its faradic irritability for considerably over a year, but the nerve loses it in 72 hours after section. The microscopical findings of Heidenhain show that all the fibres in such muscles are not destroyed, but that many are only diminished in size and still show cross striations, a finding which Vulpian and Stier (75) had previously obtained in the calf muscles of rabbits.

According to the studies of Nasse, bone atrophy also occurs after nerve section (76), but it is said to be less extreme and to occur less quickly than that in joint diseases or enforced rest (see Sudeck). This is probably referable to the longer preservation of the musculature following nerve section.

Further results of a lengthy enforced rest are *stiffening and contracture of the joints*. Pathologically anatomically, such joints develop callous and thickenings of the tissue, which show roentgenologically as dense shadows; calcification and new bone formation also occur. Briefly, the change in the connective tissue is a consequence of failing functional stimulation (Roux (1)), and less differentiated tissue takes the place of more highly differentiated structures. The stiffness which develops even after a short enforced rest, depends on changes in the muscles. According to Marey's law, the length of the red fibres of a striated muscle is proportional to the extent of the movements which the joint to which it belongs carries out, and inactive atrophied muscles are said to show a shortening of these fibres (77). In the days before bacteriology, it was debated whether these stiffenings of the joint were caused by an inflammation or a "bed-sore of the cartilage." Doubts were based on the experimental investigations of Mentzel (78). Now the question has been shelved, since it makes no difference in practice if we call the described pathological anatomical changes an inflammation or not. The main point is that they are not due

to bacteria, nor are the cases of pure immobilization, even if special investigations of the latter are lacking. The changes in joints following immobilization in plaster casts have been accurately studied in animals, and shrinkage of the capsule and ligaments was found, which, as Reyher points out, occurs later than the atrophy of muscles (see above Regnier (79)). Changes in the cartilage are to be found only when they have not been in contact during the period of rest. This again shows the significance of functional stimulation which continually wears down the cartilages. It explains why extension does not protect against joint changes, but on the contrary, separation of joint surfaces injures the cartilage.

The synovial cells are so closely related to the cartilage cells that, according to Braun, they change to cartilage in the places where they experience an abnormal stimulation. *Vice versa*, the joint surfaces often become covered with a non-vascular connective tissue layer which according to Reyher arises from the joint cartilage (80).

An accumulation of fluid in the joint after function is resumed is found in patients who have been placed at rest for a long time. Von Volkmann (81) assumed that this effusion followed tears and pulls of the shrunken synovial membrane, a view which Reyher and Moll could confirm in animals. Pathologically anatomically, the picture is that of a synovitis with swelling of the villi and synovial prolongations which resist movements.

All of these changes did not disappear in the animals even months after removal of the fixing bandages, nor did the function return to normal; an object lesson showing the gravity of placing a joint in enforced rest. The degree of stiffness in humans depends not only on the length of time of rest, but also on individual idiosyncrasies. We know that the joints of so-called rheumatics become stiff in a much shorter time than those of other individuals, and the tendency to stiffening increases with age, perhaps because the nutrition of the connective tissue is poorer and the threshold leading to shrinking of connective tissue is more easily and quickly passed than in younger individuals. In "rheumatics," we conceive of "a general retardation of assimilative and breaking down processes" (82), but exact knowledge in this field is still very meager. Further investigations are necessary to determine the status of joint stiffenings and the absorption of the new tissue in relation to Grawitz's views concerning the transformation of fibrillar tissue into cells (83). A beginning is found in the work of Bussmann (84).

The stiffened positions which joints assume when they do not perform their function on account of inflammation, or enforced rest for a time, are called contractures (85). The contracture position of the knee-joint is flexion; that of the hip is flexion, abduction or adduction. An explanation of these well known typical position anomalies was proposed by

Bonnet (Paris 1845) (86). He injected fluid into the joints of cadavers after removing all the muscles and found that when the amount of fluid reached a certain degree the joint assumed a position characteristic of its contracture position. He concluded that the capacity of the joint was greatest in this position, and that, therefore, in effusions, the contracture occurred purely mechanically by the increase of fluid. This idea is incorrect, as A. Fick (87) and others have shown, for the total capacity of a joint remains the same no matter in which position the bones happen to be, but the tension of the capsule, ligaments and muscles is changed with each change of position. The significance of the tension of these soft parts is shown by the experiments of Bonnet, however, inasmuch as he obtained these changes by injecting fluids only when all the muscles, etc. had been previously removed (88). Clinical experience also contradicts Bonnet's theory, for in marked hydrops, a joint is not always in its contracture position (89).

When a joint changes its position, some of its ligaments, and parts of the capsule and muscles are stretched and others are relaxed. There is a position for every joint in which the sum of the stretch of all the soft parts belonging to it is at a minimum. This is the rest position mentioned above, which can easily be found by discovering the most comfortable position. The sensation of comfort depends on the fact that the tension of the soft parts, particularly of the muscles, is less than in any other position, and in an effusion, the patient assumes the position in bed in which tension is felt least. In contractures, there is not simply an overbalance of single muscle groups, as Lucke (90) has asserted, but the joints become ankylosed following enforced rest or inflammation, as has been detailed above.

These reasons, correctly known to Weber (91), do not necessarily mean that a joint cannot ankylose in another position; in such a case we must look for another explanation. This applies particularly to the position of abduction of the hip in the first stage of coxitis. König (88) has pointed out that in an early stage such patients continue walking, but spare the leg by holding it in the position of abduction. In special contracture positions, particularly of the arm, the element of gravity is added, which brings the affected part in a position other than that of rest. Obviously a pathological luxation will affect the contracture position.

It is not difficult to understand the deviations in paralyses, destruction of certain muscle groups, contractions of certain muscles the site of inflammations or suppuration, or in skin cicatrices (92).

The contractures in flat foot are classified among the inflammatory group (93). In this case there are peripheral muscle contractions, but what sort of stimulus brings the muscle to such spastic positions is



unknown. A bacterial infection is, of course, excluded. Probably they are irritating processes such as arise in injuries of sensory nerves in which reflex contractures are also observed. Furthermore, such reflex contractures are often very noticeable in fractures, *e.g.*, of metatarsals (foot swelling) (94).

They disappear after rest, wet dressings and baking, usually in a few days even when the foot is so firmly fixed that there is no difference from an "organic" contracture.

It seems superfluous to use, as Herz (95) does, the comparative greater strength of the flexors as an explanation of the various forms of contracture, especially since R. Fick (5) has shown that on the contrary the extensors are definitely stronger, for example, in the knee joint, even when the flexors of the leg (gastrocnemius, etc.) are included (96).

Contractures in flexion which cannot arise from a rest position also occur, as, for example, after the patient has recovered from a resection of the knee. We also see in bed-fast patients that the contractures in later stages are in positions beyond the rest position (strongly flexed), and in such cases there is more extensive atrophy of the quadriceps than of the flexors, in other words, the flexors predominate. It is not known why the quadriceps and the gluteals and deltoids as well, should atrophy so much more rapidly than other muscles, but just as in disuse atrophy, a reflex cause has been assigned (97). Fischer (98) believes the greater atrophy of extensors is due to the stronger construction of their fascia and thus circulatory changes will occur more readily. Jansen (99) correlates it with the different lengths of the bundles and fibres by assuming that in increased tonus the weaker flexors, adductors, and inward rotators predominate, and *vice versa*, in diminished tonus. It is interesting to know that the extensors are said to have a different electrical irritability than flexors (100). Grunewald (101) offers as the reason that the extensors of the leg in humans are phylogenetically much younger and, therefore, are particularly sensitive. In monkeys, the lower extremity is as yet more a grasping than a supporting organ. But why this should be coupled with increased sensitiveness is, of course, not explained.

Practical surgery classifies all of these possible contractures into arthritic, myogenic, tendonogenic, neurogenic and dermatogenic, a classification which seems of therapeutic usefulness.

Furthermore, these contractures influence the shape of the bones. We have already spoken of the effects of the musculature on their form. The changed push and pull to which the bones in the neighborhood of a contracted joint are subjected bend them in accordance with the principles of statics and dynamics. That the spinal column and trunk are also involved is easily understood from the discussion of the effect of the



musculature on distant parts. Those conditions which we call deformities are produced in all probability by the continuation of muscle contractures and stretching (102). That such bendings can furthermore be brought about by general diseases such as rickets, osteomalacia and similar conditions, shall only be mentioned here, since, at least in their acute stage, they fall in the domain of internal medicine.

The relation of these joint changes following immobilization, to *arthritis deformans* is still debatable. At present we look upon arthritis deformans in about the same way in which tuberculosis was regarded before the discovery of the tubercle bacillus; that is, we are compelled by pathological, anatomical and clinical findings to group and identify disease pictures. Just as before the discovery of the tubercle bacillus, much was considered tuberculous which has subsequently been proved otherwise, for example, the necroses following subcutaneous serum injections in rabbits—so it is with the various chronic joint diseases.

As an introduction we must pause at the pathological anatomical findings in early cases, but it is to be expected that authors do not agree in their interpretations (103). This much is known, particularly from the extensive work of Pommer, that in arthritis deformans the regressive changes are primarily in the cartilage (p. 185 and 229) while the subchondral changes, "the extension to the marrow cavity and vessel canals" and the other changes in the bones themselves, are secondary. Axhausen describes this process very minutely. According to him, the first manifestation is necrosis of cartilage, and this is the cause of all the further changes in the joint. These aseptic necroses are not to be confused with sequestra. Pommer disagrees with Axhausen in the explanation of the necroses and considers them "consequences of the injuries done to the cells in the most superficial layer by the grinding of the cartilage and abraded areas of bones." But Axhausen bases the interpretation of his findings on very interesting animal experiments. He produced localized necroses of the joint cartilage with an electric needle, and later found all the changes characteristic of human arthritis deformans, including the spread of the localized reaction to the whole joint, in which respect it is still more comparable to the arthritis deformans of man. It cannot be denied that these experiments are convincing. Pathological anatomical findings parallel the changes for us, by experiment we can follow them as they occur, and it is certainly shown by his experiments that an injury leading to necrosis of the cartilage may initiate all the pathological anatomical changes which we consider characteristic of arthritis deformans. That distinct forms of arthritis deformans may develop in this way was shown by Axhausen (103) in three cases in which, following injury of the knee joint, there was found a localized necrosis of the cartilage at the site

of injury and around it, hyperplasia of subcartilage marrow, rim osteophytes, tags of synovia, etc. These experimental studies place a new aspect on the long known fact that arthritis deformans can develop after injuries. The injury causes the necrosis of cartilage, but the fact that the arthritis develops much more frequently after luxations than after other types of injury (103), is not completely explained. Thus far it has never been demonstrated, although it seems reasonable that damage to cartilage is particularly likely to occur in dislocations (Axhausen). In opposition, the experiments of Magnus (104) and the pathological anatomical studies of Tashiro (104) show that in suppurative inflammation of joints and similarly in gonorrheal arthritis, many cartilage necroses arise, and while a true arthritis deformans is rare, these often lead to an ankylosing arthritis. The relationship of arthritis deformans to these necroses is not altogether clear, but it cannot be concluded that it will develop whenever necrosis occurs. The studies of Gies (105) give general information on the healing of injuries to cartilage.

To approach the investigation of the etiology from the clinical standpoint, it is necessary to clearly define what chronic joint diseases shall be considered arthritis deformans. Pommer on the basis of his anatomical studies does not include ankylosing joint inflammation (103, p. 232), but considers senile hip arthritis, as arthritis deformans. Therefore, when Stempel (106) describes senile hip arthritis as an ankylosing hip joint inflammation, he departs from the customary nomenclature and this leads to misunderstanding. It seems necessary to adopt Pommer's strict anatomical classification before progress can be made in this difficult subject.

It is hard to explain the so-called spontaneous arthritis deformans; in the case of "secondary" arthritis deformans, we always have the time of injury, trauma or suppuration, from which to date the reactive processes. Even if we take the views of Axhausen as a basis, we cannot evade the question of how necrosis of the cartilage can occur without trauma. In the arthritis of youth, there is, of course, infection, but the discussion of the exciting causes is not necessarily exhausted with this.

There are two other theories, both proposed in the last few years, the one of Wollenberg (103), which regards it as a consequence of nutritional disturbances of the cartilage with particular reference to arteriosclerotic changes, and that of Preiser (107), which places the responsibility on changes in the statics of the joints. Wollenberg believes that chronic local disproportions between arterial supply and venous return initiate the various regressive and progressive manifestations, and that the undernourished bone reverts back to cartilage which needs less nutrition. The blood supply, too small for bone, is now too abundant for cartilage, and

the latter becomes hyperplastic. This theory might have been fruitful, but it was developed to too minute detail, and thus was laid open to opposition. The principal reason which may be brought against it, is that in arthritis deformans the arteriosclerosis is not confined to the diseased joint, but is general and it seems inexplicable that the changes should be localized to one joint. Pommer believes that the changes in the vessels are secondary. To support his views, Wollenberg also had recourse to animal studies; he shut off the circulation of the patella of a dog by circular punctures around the bone. After a time, he found changes which he considered indicative of arthritis deformans, a conclusion which was immediately questioned (108). By control experiments it was demonstrated that the changes found in the patella were only the reaction to a coincident injury to the bone, or to necrosis of the cartilage, or simply to pure inflammatory processes. At any rate, these experiments gave no evidence for the arteriosclerosis theory, and Wollenberg's views have little in their favor.

From his investigations on the changing position of the acetabulum, Preiser (109) reached the conclusion that pressure of the head of the femur on an unusual place or unevenness of the joint surfaces would lead to the disease (improper static relation). In later work (107) he leaves the question open of whether these static anomalies injure the joint directly or through the blood vessels.

Kroh (110) investigated the theory by changing the static conditions of the joints of animals by all sorts of intra-articular manipulations. He actually obtained marked deformities, which not only remained localized, but spread to the whole joint and showed a tendency to progress. But it is questionable, if such severe intra-articular manipulations may be taken as confirmatory evidence of Preiser's "static" theory.

In humans, also, it has been observed that an arthritis deformans often develops in such falsely weighted joints (*e.g.*, genu valgum); on the other hand, as König (111) particularly pointed out, arthritic alterations occur in joints which show no static displacements.

If the conditions of pressure within joints are of such significance, it is pertinent to ask if an increased pressure of long duration could not initiate these changes. We know a few of the mechanisms which ease the bumps and shocks of movement in a joint (112); in addition to the cartilage and the rims of cartilage, they are the synovial membranes, the fat, tendons and ligaments, and last, but not least, muscle tonus. On these as a whole, depends the "elasticity" of the movements. Whether it is diminished in those individuals, perhaps with a constitutional peculiarity, who show a tendency to arthritis deformans, is not known at present. But the possibility cannot be disregarded, and a search has been conducted for tend-



encies toward gout or changes in calcium metabolism, etc. (see Wollenberg (103), p. 413). Lane (113) speaks of a "scrofulous" or "strumous" disposition. There is an inheritable bodily condition which favors the development of gout, obesity, diabetes, calculi, arteriosclerosis, rheumatism, etc. (Bauer (82)), but in spite of many attempts, arthritis deformans has never been shown to be related to gout (114).

The senile chronic deforming joint processes are usually distinguished from true arthritis deformans (see Weichselbaum (115), Axhausen (108)).

We can, therefore, sum up the present state of our knowledge by saying that those cases which arise after injury are well explained by the experiments of Axhausen; that there are cases, however, in which an injury cannot be demonstrated; further, that the severity of the joint changes is not simply proportional to the severity of the injury. This means that some, as yet unknown factor, other than cartilage necrosis, is concerned.

The development of a *joint mouse* bears a certain relationship to arthritis deformans. Since Monro (116) in 1726, first found a body in the knee joint of a woman, who had a defect in the external condyle of the femur, injury as a cause of free bodies in the joint has again and again played a role in the literature, although it was much combated by Laennec and his students. There are several reasons which may be enlisted in opposition to this theory of the traumatic origin of loose joint bodies. In the first place, a history of trauma is usually absent, or it is at most only insignificant, and such as might occur almost daily. In the second place, the trouble does not begin, as a general rule, in immediate association to an injury but months and years afterward. The shape of most joint mice is incompatible with the theory of their traumatic origin. As König remarks (117), pieces of cartilage may be torn loose and remain hanging to joint tendons, but they would not appear as "flat pieces from the outer surface of articulating bone ends." Careful pathological anatomical studies have shown that this view is correct. "Up until the present, there has been no case recorded which showed that a flat arthrophyte arose by primary detachment following a single trauma" (118). On the other hand, the studies of Budinger have shown that partial detachment of cartilage is not uncommon, and it is at least conceivable that such partially loose bodies may become completely detached by movements of the joints. At any rate, the material Budinger used for study was derived from such severe traumatism that he doubts the value of his own cases. Poncet and Kragelund (119) were able to cause small pieces of cartilage to fly off, by directing tangential blows on the knee joints of cadavers. Others succeeded in producing joint mice by injury to animals, but found that such detached pieces almost always became attached to the wall of the joint (120). The bony part dies, and accord-



ing to Bier (121) is absorbed by the synovia; the cartilaginous part remains living, a finding which is also true of the joint mice of humans. Still it is incorrect to conclude just because of the agreement in the histological findings in man and animals, that the loose joint bodies in man are detachments. Cartilaginous tissue has great tenacity of life and resistance, as shown, for example, in the transplantation experiments of Seggel (122). Bier (121) calls attention to the fact that loose joint bodies are generally covered all around with cartilage which is supposed to protect it from the solvent action of the synovial fluid.

In the joint mice of humans, the first thing to explain is the time element, why a piece of cartilage becomes loose years after an insignificant injury. Is there an actual causal relation between injury and joint mouse? The work of Marten (123) illustrates the clinical course on this point. Cases coming to autopsy showed that there were occasional localized necroses of joint cartilage which led to the demarcation of a fragment of cartilage and bone (124), and as the preparations of Klein (125) showed, to the formation of a loose joint body. But the question still remains of whether this form of cartilage necrosis and the subsequent appearance of joint bodies are the usual course of events and whether there is a relationship of injury to later demarcation of the cartilage. Konig, who has given the name *osteocondritis dissecans* to this pathological process, believes that a mild injury may damage a localized place severely enough to lead to necrosis; a later "dissecting" inflammation loosens and separates the part. At the same time he believes that there is a spontaneous osteochondritis dissecans, the causes of which are still obscure, but which arises without previous injury and runs the same pathological anatomical course. Ludloff (126) supports the opinion that such an osteochondritis might arise from injury to blood vessels. It occurred to him that in the cases involving the knee joint, the osteochondritis always developed at one circumscribed spot, namely, on the internal condyle of the femur near the insertion of the posterior crucial ligament, and he tried to discover by x-ray and anatomical studies a special peculiarity of the blood vessel distribution of this place (127). These considerations have, however, been contradicted (Kirschner (128) and others), even if the clinical observations were correct.

These ideas of a cartilage necrosis leading to a dissecting osteochondritis were supported and elaborated by Axhausen on the basis of his above mentioned animal experiments, and pathological anatomical studies (103). By pricking the surface of the joint with an electric needle, he could obtain necrosis of cartilage and the same demarcation process in the bone as is found in human osteochondritis dissecans and its sequel—changes in the entire joint—as was mentioned above. He believes accordingly,

that the production of joint mice and arthritis deformans may be regarded from a similar point of view; the primary process is always a necrosis of the cartilage which may be caused by a mild trauma. As a consequence, there is separation by a process of granulation, and a formation of joint mice or arthritis deformans. Whether primary necrosis of the cartilage may be caused by something other than trauma remains an open question (vide supra).

It is quite logical to believe that a joint mouse may break off in a well marked arthritis deformans (129) and that by continuous irritation of the joint, new necroses may occur and new fragments be freed. Furthermore, such loose bodies may arise from cartilaginous tags or parts of the capsule (Fischer (129)).

These loose bodies may grow even if they are free in the joint. The histological processes which may finally lead to three fold increase in size were found to depend on "periosteal apposition" and on "cartilage proliferation" (130). According to Schmieden, the connective tissue of the dissolved bony part seems to play an important part, and regressive processes, especially necrosis of the cartilage, are demonstrable in its vicinity. The necessary nutrition must be procured from the surrounding synovial fluid, possibly as in plasma cultures of tissue. There is a certain similarity in the growth of a joint mouse and the growth of the head of the radius when the latter is dislocated and not replaced. It might also be called an example of how cell growth is held in check and regulated by function. If the articulating end of a bone escapes from its ligaments, the restriction to growth is removed and that part of the bone may grow disproportionately. In the case of the head of the radius the nutrition comes, of course, wholly through its blood vessels.

That muscles should undergo necrosis, that there should occur what we know as gangrene when all the vessels are ligated, is not difficult to understand. Pathologically physiologically of far more interest are the consequences of diminished nutrition which leads to connective tissue replacement and to the so-called *ischemic contracture* (131). Insufficient arterial supply with venous stasis has long been accepted as the cause of these changes in the muscles. Many lay particular stress on the venous stasis and its consequent carbon dioxide poisoning (132). If this view is correct, it should be very easy to produce an ischemic muscle contracture in animals. And yet this is not the case. Shutting off the arterial flow, as for example, in the so-called Stenson's experiment (ligation of the aorta) (133), or the application of a tourniquet to the thigh, indeed leads to a breaking down of muscle fibres and nuclei, and functionally, to the beginning of a stiffening, as the description of Heidelberg has shown. But if the animals are later allowed to run around, the muscles quickly recover and

regenerate. The same result is obtained after ligation of veins (Kroh), and clinical experience has shown that ligation of the femoral vein which is often done for pyemia (134), does not lead to ischemic contracture. Circulatory disturbance alone, therefore, is not sufficient to bring this about.

Unless the affected limb is placed at rest, and indeed it need not be bandaged, the inactivity alone suffices to produce the described changes. Clinically, the cause of circulatory alterations in particular cases may be varied. Ischemic muscle contractures are mainly seen following supra-condylar fractures of the humerus and in fractures of the middle of the forearm (135). In the first case, a tearing of the intima of the cubital artery often occurs or a mechanical compression of this vessel by the displaced fragments. In fractures of the forearm, as Kroh has shown in a case of crushing, a hemorrhage may force the musculature into a typical contracture position and lead to the circulatory disturbance.

The venous stasis and the edema increase not only the circulatory difficulties, but also the inactivity of the muscles. Bardenheuer calls attention to the venous "suction cups" lying in the bend of the elbow, therefore the flexors particularly are damaged.

*Venous stasis* is of practical surgical interest from other viewpoints than simply that of circumscribed ischemic musculature. We see, for example, how the flap in plastic operations becomes swollen and blue when turned on its pedicle. The thin walled veins are more or less kinked, the venous blood cannot flow out freely, carbon dioxide accumulates in the free edges of the flap, and the capillaries are compressed by the swelling. If no further therapeutic measures are undertaken, the edges become necrotic, but simple puncture allows egress to the venous blood and the vitality of the cells is preserved. Similar conditions are met elsewhere in surgery, *e.g.*, in fractures. Here also we may improve the disturbed local circulation and prevent gangrene by allowing the obstructed blood to escape.

Such edema in the muscles is a hindrance to normal movements, and attempts are made to relieve it by massage. The justification is shown by the observation of Kroh, but its importance must not be overestimated. For example, Kroh terms the conditions in stiffness of a muscle after exertion as "greater blood stasis and transudation;" as proof, he calls attention to an increase in its volume, but this explanation seems too mechanical. How insignificant is the functional diminution of the musculature in the edema of nephritis. Edema is often the expression of a diseased condition in the vicinity of musculature, and not the primary cause, although, of course, it may further damage its function.

Under the influence of v. Volkmann's work on ischemic muscle contracture, *participation by peripheral nerves* was disputed for a long time,



and a sharp distinction was made between damage to muscles by nerve injuries, and by interference with circulation. It was supposed to be characteristic of ischemic muscle contracture that the muscle could still be electrically stimulated through its nerve, while the direct electrical irritability had long disappeared. In spite of this, a participation and injury of the nerve cannot be denied, in fact, in many cases, it must be considered of causal importance in the development of this disease picture, since by its involvement, the damaging inactivity is increased. That tight bandaging, *per se*, reduces the sensation in an extremity is an observation which can be made daily in operative cases, and which has been examined experimentally by Neugebauer, Kroh and others. To eliminate the effects on the nerve trunk of the pressure of a bandage, Kroh compressed his own brachial artery and obtained a distinct sensory disturbance in his hand in 12 to 14 minutes. More interesting is an observation of the same author, who, after isolated compression of the femoral artery, noticed a distinct disturbance of sensation in the area supplied by the sciatic nerve. This shows how closely nerve conduction is related to circulatory disturbances. In animals, he often observed a complete motor and sensory paralysis in the distribution of single nerves of the leg after ligation of vessels. In ischemic muscle contractures in humans, Bardenheuer, Hildebrand, Kroh, and many others often demonstrated sensory disturbances quite conclusively.

The damage, therefore, comes from two sources, blood supply and nerve supply. In the well developed case, the nerves can be pinched by the connective tissue and further hindered in their activities. To remedy this condition, Hildebrand transplanted the nerves and obtained good results.

Ischemic muscle contracture in its details, is, therefore, considerably complicated, but the basal causes arise from circulatory changes and inactivity. The importance of plaster casts in the production of this condition must, therefore, be judged from this viewpoint and it should be particularly remembered that it is not necessarily the result of a bandage which is too tight or binding, but that it favors contractures because it keeps the muscles at rest. The circulatory element, *e.g.*, rupture of the intima of an artery, may add to the trouble if it is applied too tightly or if the limb subsequently swells.

A congenital disease which must be considered from the microscopical appearance of the muscle as an ischemic contracture is *torticollis* or muscular wry-neck (136). This idea has been generally recognized only since the work of Voelcker (137), who observed a number of changes in patients with wry-necks, such as a deformity of the ear muscles, which indicate that the child's head had already assumed an oblique position



in utero. This position of the fetus leads to pressure on the artery of the sternocleidomastoid muscle and thus the fundamentals for the production of an ischemic muscle contracture are fulfilled. Schloessmann (138) confirmed the views of Voelcker. The other theories of traumatic or inflammatory origin are contradicted by the pathological anatomical findings which indicate an ischemic origin.

Another disease of muscles which reduces their freedom of movement is concerned with bone formation; *myositis ossificans*. We know from normal histology that bone may arise not only from periosteum but also from connective tissue. In myositis ossificans, the question of the histogenesis of the bone has played the leading role.

In general, a division is made between a progressive and circumscribed myositis ossificans. The former has been of only casual interest until recently. It is thought that there is a constitutional anomaly; the tissues have less ability to become more highly differentiated and arrive at full development, but the nature of the process is not known in detail. It is not hereditary, but such patients often show other degenerative processes. Up until now, there have been from 70 to 80 cases published, mostly in surgical literature (139). Symptoms may be improved by removing irritant bone particles, etc., but the course of the disease is not influenced in the least.

Localized myositis ossificans is of far more interest and practical importance. The question arises, however, whether all the conditions included under this term are really pathologically similar to it or to each other. The fact that bone tissue appears in lungs, testes, lymph nodes and muscles, does not necessarily justify the belief that these pathological processes are alike.

The cases of myositis ossificans circumscripta which are being subjected to much discussion at present are those which develop after injury of the supporting apparatus, *i.e.*, when there are pieces of bone in the muscle in the close vicinity of the site of an injury (140).

Still other types of cases, intermediate one might say, are those in which an injury has occurred to tissue with no recognizable relation to the skeletal system. These are, for example, the bone formations in laparotomy scars, such as have been described by Ropke (141). Here we can only conclude from the rarity of its occurrence, that there are individuals whose tissues are peculiarly prone to bone formation, but we have at present no idea of the nature of such a disposition. We very often meet with such differences in wound healing in our patients. Some have tight scars, others soft, some develop a large callous, some a pseudo-arthritis, some are predisposed to keloid formation, and so on.

At present, it is not possible to correlate these different healing tenden-

cies with the "types" elaborated by the studies of constitutions. It has been frequently asserted, of course (Wilms and others), that people with the "arthritic" or "rheumatic" diathesis are more liable to connective tissue growth and cicatricial contractures, but it is easy to discover opposing observations. Judgment in all these things is so difficult because of the many uncontrollable outside factors which interact in the firmness of a scar, such as slight deviations in the method of injury, etc. The healing of the aseptic operative incision is, after all, a remarkably similar one in the many patients who are daily operated. Deviations in the healing process occur only in those suffering from some general disease (142). In infected or crushed wounds, the conditions are different. Old axioms of the laity which speak of a "good or bad healing skin," have much justification, but we can hardly investigate this scientifically, because of the difficulties in evaluating outside factors such as virulence of infection, tissue destruction, etc. That these outer factors do play a role was made evident in large numbers of cases during the war (see among others, Voelcker (143)).

There are a few special situations which the process seems to elect. Following luxations of the elbow, the bone formation is often quite typical in places at which the periosteum has been torn off with pieces of joint capsule (144). The so-called horseback rider's, infantryman's, or bayonetier's bones owe their origin to coarse tears of the muscle with possibly a partial pulling off of the muscle from the bone. There is a difference of opinion as to whether this bony foundation in the muscle arises from detached threads of periosteum or from connective tissue (145). That periosteum detached from bone is capable of producing new bone is a well established fact, shown by taking fragments or suspensions of finely divided periosteum and introducing them into the muscles or soft parts (146) when cartilage or bone formation results. The conditions applying to traumatic myositis ossificans were imitated quite accurately in animals by Berthier, but it has never been possible to produce a progressive growth of bone. It may be due to a difference in the tissues of animals and man; indeed dogs are far less useful than rabbits in such bone formation investigations. It cannot be concluded that the subject is exhausted by accepting detachments of periosteum as the cause of the disease. Sudeck and Pochhammer are of the opinion that the method of growth, particularly the duration, points to a periosteal origin of the bone, since heteroplastic bone transplants develop differently. This opinion is contradicted by Gruber, and is really not entirely satisfactory.

The two views are again and again expressed as various workers enter this field; the one, that the bone fragments are entirely separate from the main bone of the extremity and develop in the substance of the

muscle, a point for its connective tissue origin; the other lays stress on an injury to the bone, and accepts the experimental result even if it is not entirely established, that there is growth from detached fragments of periosteum, which are supposed to be scattered far into the muscles (147). Why could not the circumstances be similar to those in the formation of callous? In this process, there is first an hyperplasia of connective tissue, which is not penetrated by a growth of periosteum, but, according to the prevailing opinion, by "direct metaplasia turns into reticulated bone" (2). That this metamorphosis does not result independently, but is influenced by periosteum and bone marrow is naturally understood. The latter, however, do not rebuild the bone themselves, but by a sort of indirect influence bring this end about through the medium of connective tissue. How much of this influence is owed to the blood supply, which according to Lexer and Delkeskamp (148), arises from the vessels of the periosteum, that is, from the tissue chiefly concerned in the formation of bone, is not known. But we do know that fractures heal badly when the circulation is disturbed (44). Probably we are justified in considering that such an indirect influence acts in myositis ossificans traumatica, a belief which will allow the opposing views on the histogenesis of the disease to be better correlated.

Bone formation may perhaps be favored by the hemorrhage because of nutritional disturbances in the injured tissue (Bier (149), in opposition to Hildebrand (149)). At least, Liek (150) showed that bone formation took place in the kidney after ligation of its vessels.

When all is said, however, it still remains inexplicable why this bone formation should occur so rarely. Many people ride, yet few develop myositis. Is it because there are small differences in the manner of injury, or does it reside in differences in individuals, that is, to a special "predisposition" (Kuttner)? That there are variations in the ability to form new bone is shown in any active surgical practice. The examples given by Kuttner seem to make it probable that these different predispositions have definite significance in myositis ossificans.

This method of discussion now leads to a consideration of the bony overgrowths following nerve affections. Wilms (151) called attention to the bone formation in the muscles of tabetics which occur in addition to the arthritic changes. He declares that these changes are found primarily in those muscles which are attached to joints held in contracture positions; and thus it may be an injury which causes the bone formation. Later observers concur that these changes are found quite commonly in many other nervous diseases (152). Some could indeed find them in bedfast patients in whom every possibility of trauma was excluded, but

whether the condition is inflammatory or is a growth disturbance due to nerve paralysis, has not been determined (153).

## NERVES

The surgery of peripheral nerves has gained in interest and importance through the problems of the war. Many theoretical questions have arisen, especially in connection with the *healing of nerve wounds*, and the subsequent restoration of function.

We may accept from the embryological studies of Hiss and the experimental work of Harrison (154), that all nerve fibres grow from ganglion cells and that following injury, the peripheral part of the nerve degenerates and a new nerve arises by the outgrowth of the central portion and subsequent union with the peripheral portion.

This growth of the central end begins immediately after the injury, but necrotic tissue, blood, granulation tissue, or lateral displacement of the stump, prevent the outgrowing fibres from finding the peripheral ends. The fibres grow into the tissues, obstacles change their course, and so they lose their direction. In this way a neuroma and a thickened scar around the wounded nerve develop. Neuromas may be prevented in amputations, by crushing the nerve and closing its sheath so that the separate axis cylinders cannot grow (155). As soon as the fibrils from the central and peripheral ends touch or when their union is accomplished by suture, there again ensues a functioning nerve fibre.

The previously accepted view was that the central end grew into the peripheral end, under the direction of the ganglion cell. But according to Bethe (156), this is untrue, for the central stump enlarges only a few centimeters and particularly in younger individuals, the peripheral part can regenerate completely before it joins the central stump. Such "auto-genous regeneration" does not lead to a permanent nerve, because this newly grown peripheral part degenerates, but there is justification in the assumption that in permanent regeneration the central end does not simply grow into the peripheral piece, but that the latter takes an active part through a "stimulatory action" of the former.

Such a severed nerve can grow not only into its peripheral portion, but the surgical experience of the last few years has shown that it can grow directly into a muscle into which it has been transplanted (157). New endings develop and the muscle is re-innervated (neurotisation). (The work of Erlacher (158) gives anatomical data regarding the nerve endings in muscles.)

This fact is of great biological interest, reminding us of the ingrowth of nerve fibres in embryonal life which has been studied particularly well by



Braus (159). He transplanted the buds of extremities to either the head or tail end of the embryo of amphibians shortly after their appearance and before nervous elements had appeared. By this means the bud came under the influence of "strange" nerves. A completed limb arose and what is more remarkable, the motor nerves wandered in, and innervated the muscles. In like manner, the sensory nerves developed independently of the motor nerves. Furthermore, the branches of the nerves were exactly similar to those in a normal extremity. The forces which bring about such a phenomenon are unknown, but there are analogies in other tissues, *e.g.*, the metamorphosis of ordinary ectodermic cells to true lenses (eyes) when the ectodermic cells are brought into contact with the optic vesicle (Spemann, cited by Braus). The contact of tissues is sufficient, therefore, to stimulate such growth. Similar forces are probably concerned in causing the nerves of adults to wander into and supply an otherwise entirely strange muscle.

It is also possible to unite two different motor nerves in adults, as for example, to transplant the accessorius or hypoglossal to the facial, in facial paralysis (160); in fact, the motor hypoglossal may be united to the sensory lingual; after which an outgrowth of hypoglossal fibres occurs, with partial, if not complete, innervation of the tongue (161). The first of these experiments was done by Flourens (cited by Bethe), who severed both branches of the brachial nerve of a fowl and sewed them together crosswise. Elaborate experiments of this kind were carried out by Spitzzy (162) who hoped that his results could be used in infantile paralysis. There are many possibilities in nerve grafting, and although the practical results have been none of the best, their theoretical foundation is, of course, not disturbed. These operative and experimental results show the extensive ability of the human locomotor apparatus to learn new functions. The facial or motor trigeminus in the experiments of Braus, were used for the nerve of an extremity, and the nerve of the tongue, when grafted, can learn to move the muscles of expression of the face. This learning of a new function as in a transplanted muscle occurs in the centers.

The separate strands of the peripheral nerves are not isolated in their course to a ganglion but anastomose freely with one another. Nevertheless, it is possible to trace a degenerated strand in cross sections of the nerve, high up in the plexus, *e.g.*, after extirpation of a muscle (163). These individual strands do not always occupy the same place in a nerve, as Stoffel (164) states, but change their positions in individual preparations (165).

The motor nerves can be stretched to a certain extent without showing changes in function, but the amount as stated by various writers differs. Six centimeters may be taken as the upper limit (166), corresponding to

from 24 to 38 per cent. of their length. It must be remembered that stretching also loosens the nerves, and probably most of the stretching is spent on surrounding tissues and hardly any on the nerve substance itself. But obviously there must be some room for play, when, for example, we flex the knee joint, the sciatic is much less stretched than when it is extended. During flexion the nerve has also a slightly tortuous course, which Stoffel (167) demonstrated in monkeys by fixing the tissues *in situ*.

With the exception of severing of nerves, the most important conditions requiring surgical interference are *neuralgias* (168) and *neuritis*. Curiously enough, nerve injuries on the whole cause little pain as the accumulated reports of the war testify. Patients seldom complain of troublesome sensations in a paralyzed limb, as in amputations. Why they are present following amputations and usually absent in gunshot wounds of the nerves, is unknown. But there are individual cases of the latter in which exceptionally severe pain is felt (169). According to Popper, it usually follows penetrating wounds of the plexus or high up on the sciatic, that is, in injuries near the spinal cord. He assumes that a concussion reaches the centers, as evidenced by vasomotor phenomena, and that inflammatory irritation is superadded. According to Schlossmann, a neuritis actually arises at the site of the wound. Perthes (170) could show that freezing of the nerve above the site of injury was sufficient to block the conduction and allay the pain.

Following such pain, contractures in neighboring muscles result with rapidly increasing stiffening of the joints, the contractures being due probably to reflex disturbances (171). The part played by such "reflexes" in joint stiffening has already been discussed.

True neuralgia has also been the object of operative procedures. The methods designed to destroy or remove a diseased nerve do not interest us here. The open method for nerve stretching has given opportunity to study many changes which have been regarded as immediate causative factors. Thus varices have been described (Quenu), narrowing of their paths, *e.g.*, through foramina (Bardenheuer), inflammatory growths (Renton), pressure from enlarged lymph nodes (Partsch (172)), etc. But all of these anatomical changes have been the exception, the majority do not show such gross mechanical causes. Edinger states that the primary cause is a functional change in the vasomotor nerves of the vessels which supply the nerve and the pain is supposed to be incited by a change in the blood supply.

Elaborate studies of the effects of nerve stretching on neuralgia have been made, but we have arrived at no clearer understanding of the problem than to say that after stretching, the nerve is loosened from its adjacent

tissue (neurolysis), and certain modifications of the nerve substance have occurred similar to tuning a violin string (neurokinese (173)). The statement is made that the sensory paths are made non-conductive more quickly than the motor paths. Whether this actually takes place remains to be investigated. The fact cannot be denied that certain nerves recover after injury much less readily than others. Thus, *e.g.*, the peroneal portion of the sciatic nerve remains paralyzed much longer than the tibial part, according to Hoffmann (174), because the former has a poorer blood supply.

Neuropathic bone and joint diseases are closely related to arthritis deformans. The principal pathological anatomical difference lies in the fact that in the former diseases the soft parts surrounding the joints take part in the process (175). As has been mentioned in connection with myositis ossificans, the joint changes in nervous diseases are particularly grotesque. Von Volkmann (176) believed that the destruction became so severe because sensations are diminished and patients walk about with slight injuries, and thus traumatize the joints all the more. Charcot (177) states, on the other hand, that some sort of a trophic nervous influence must be concerned. His general anatomical findings have not been confirmed by later observers (178), and muscle atrophies seem to be exceptional (152).

We have touched upon the question of trophic nerves in speaking of muscle atrophy in joint diseases. Similar considerations suffice for the bone atrophies in paralyses. That a paralyzed limb lags behind in growth can be seen in poliomyelitis. It has not been decided whether there is a specific trophic influence at work or whether the growth disturbance is only a consequence of the enforced rest from paralysis. The animal experiments in which mixed nerves like the sciatic were severed, throw no light on the subject (145).

Since the diseases in which such trophic changes appear (tabes, syringomyelia, spina bifida, etc.) chiefly affect the sensory nerves, experiments were devised to find a relation between the degree of pain sensitivity and the reaction of the body to invading injurious substances (inflammation). It was soon found that there was a definite relation between the condition of the blood vessels and sensation; and these views are supported by observations in local anesthesia.

The influence of cocain was first made use of in ophthalmology (179). Later Spiess (180), after observations on the mucous membrane of the nose, built up his theory of the influence of pain in causing inflammation, but on the whole, his ideas have not been accepted because they are too hypothetical. In surgery, it was observed that a spina bifida, etc., did not take part in the reactive hyperemia following the removal of an

Esmarch bandage on the leg, which called attention to the relation between sensory nerve paths and vasomotor nerves. In nerve injuries, as Breslauer (181) points out, the immediate results of section must be differentiated from the later results. In the first eight days (study of Bier (182)), a change in the vasomotor reaction does not take place; later, the ability of vessels to actively dilate after peripheral stimulation is lost (mustard oil experiments of Bruce (183) and Breslauer), while vasoconstriction remains intact. Breslauer concludes from studies on patients with gunshot wounds that these defective reactions of the vessels are also guilty in the production of trophic disturbances, as, for example, perforating ulcers, etc. Reactive hyperemia is, of course, a protective mechanism, and it is absent in an extremity with sensory paralysis because the vasodilators are injured, that is, the vasodilators belong to the cerebro-spinal system, the vasoconstrictors to the sympathetic (Breslauer). The same explanation is given by Trendelenburg (184) for the finding that in pigeons after section of the posterior roots, the feathers on the operated side grow much more slowly than those on the other.

### OSTEOMYELITIS

Our knowledge of osteomyelitis as a distinct entity dates from quite recent times. The first description is by Chassaignac in 1853, following him came the works of Demme, Gosselin, Boeckel, Roser, Waldeyer, Volckmann and in the year of 1874, those of Lucke (185). The first experimental attempt to discover the nature of osteomyelitis was made by Rosenbach (186), in 1878, who allowed all sorts of physical and chemical irritants to act on the bone marrow, finally arriving at the conclusion that bone marrow phlegmon could be produced by no kind of irritant except of infectious origin. He was also the first to obtain an osteomyelitis of hematogenous origin, without particular interference of the general well being, by direct injection of pus into the blood stream, after fracturing a bone. On the whole, Kocher (187) confirmed these results by similar experimental procedures, only a short time after Rosenbach. But Kocher believed that the condition could arise from the absorption of decomposition products from the intestinal tract, a view which he tried to support by the injection of solutions of caustic potash into the marrow of a traumatized bone. After the wound had healed, he added an infected and putrid calcium solution to the food. The animal then developed a subacute osteomyelitis in this leg. At that time, the nature of the irritants causing osteomyelitis was not clear, for easily understood reasons, since pure cultures of *staphylococcus pyogenes aureus* had not been isolated by Becker until 1883 (188), and shortly after, Rosenbach cultured



osteomyelitis pus, by the methods of Robert Koch which were just then published. With pure cultures of staphylococcus at hand, experimental efforts to produce osteomyelitis followed in rapid succession (189), with the uniform finding that it was possible, particularly in young rabbits, to produce an osteomyelitis very similar to that in man by the injection of pure cultures of staphylococcus in the ear veins, and that a mild trauma, such as tapping the bone was helpful in the production of the condition.

We can picture the action of trauma by assuming that the injury diminished the bactericidal substances. Either the bacteria settle at this "*locus minoris resistentiæ*," or the trauma strikes a bone in which the bacteria are already present, but harmless.

Later bacteriological examinations of the pus showed that it was not only the yellow staphylococcus which causes this disease, but all pyogenic organisms have the same ability, that is, staphylococcus albus, or citreus, streptococci, colon bacilli, b. typhosis, pneumococci, pneumobacilli, b. influenzae, gonococci, etc. These studies have established, then, that acute osteomyelitis is an hematogenous infection of the bone marrow usually by the staphylococcus. The question immediately arises of why the bone marrow, particularly that of children, is so predisposed to suppuration, when the cocci are present in the blood and reach all the other organs of the body in the same manner. As a reason, the first factor suspected was the distribution and size of the blood vessels. Lexer, Kuliga and Turk (190) and others have carefully injected the vessels of bones and photographed them with the x-rays, by which means a good idea of their distribution can be obtained. Lexer assumes that groups of staphylococci do not reach the smallest capillaries, but remain clumped in the vessels of somewhat greater calibre. These larger vessels are found in the middle portion of the bone, while the vessels toward the epiphysis become smaller. It so happens that the capillary network in the middle part is particularly richly branched. These would all be factors favoring the deposit of the staphylococci in this situation. Bacteria which are thought to travel singly and not in clumps, in the blood stream, e.g., the tubercle bacillus, reach the epiphysis and are halted in the finest branches. This theory seems very illuminating, but certain opposing considerations cannot be ignored. In the first place, we know of parts in the human body where the slowing of the blood stream can be much greater than in the bone marrow, and where, in spite of this, a hematogenous suppuration practically never arises, for example, in the corpora cavernosa; furthermore the studies of Bier (191) and his students have shown that hyperemia tends to inhibit infection. This latter point is prettily shown by the studies of Samuel (192) and Roger (192) in which after producing hyperemia in the ear of a rabbit by section of the

sympathetic, they found that it was most difficult to infect it, while it became infected easily after section of the auriculotemporal nerve.

The manner of distribution of the blood vessels can influence the deposition of bacteria to a certain degree, but it cannot be the only and final cause of the development of osteomyelitis. Other factors are concerned whose details are not known, but perhaps the presence of chemical affinities between tissues and bacteria is the key to the riddle of the susceptibility of certain tissues to inflammatory changes. Many examples may be gathered from surgical pathology. There are patients who always suffer from osteomyelitis of special bones, for example, the metatarsal or metacarpal bones, and it is also well known that patients with suppurative arthritis frequently develop metastases in other joints. Experimental pathology also offers numerous examples of this process. Thus, Rascinski describes a strain of dysentery organisms which he injected subcutaneously or intraperitoneally with always the same grave changes in the intestines only.

We know, particularly from the studies of E. Fraenckel (193), that bacteria may frequently be present in the bone marrow as well as in other organs without demonstrable reaction on the part of the tissues. There must be still another factor to initiate the real disease of the bone marrow. The bacteria remain quiescent as long as the protective forces of the organism and the toxins of the bacteria are in equilibrium. It would, however, be erroneous to conclude that osteomyelitis occurs only in a weakened individual, for on the contrary, a severe local reaction such as an acute osteomyelitis, may be an expression of a particularly high immunity of the entire organism against the invading bacterium. This much has been established by animal experiments; the subcutaneous injection of diphtheria toxin in a guinea-pig with low immunity is followed by severe local inflammation and necrosis of the skin, but the final result is not fatal, while a control animal shows no local reaction, and yet dies. On the whole, our knowledge of antibodies and what we should understand by them, why one individual should fall a victim so easily to osteomyelitis and another not, is still very incomplete. But the view that its development is the result of simple lodgement of bacteria in the bone marrow is too one sided and inconclusive.

The histological changes and the course of an acute osteomyelitis depend in largest measure on the type and virulence of the bacteria, by which we mean not only the peculiarities of the living bacterium, its metabolism, etc., but also peculiarities of the dead bacterium, especially of its endotoxins, for it is well known that dead bacteria or their extracts may produce pus (194).

Antibodies are found in large amounts in the serum since the bone

marrow is the chief laboratory for their production. They are named agglutinins, bacteriolysins, hemolysins, the latter of which are of practical significance in the diagnosis of osteomyelitis (195).

In the bone marrow itself, the bacteria may bring about pathological anatomical changes of the most varied degree from violent suppuration to connective tissue overgrowth. It is also possible to imitate these varied forms experimentally by the injection of bacteria (196).

In the further course of osteomyelitis there begins the formation of sequestra. This necrosis of a circumscribed part of a bone in a living body has kept authors busy for a long time and supplied material for extensive experiments.

As early as 1855, Hartmann (197) produced bone necrosis with sequestrum formation by blocking the nutrient foramen with a sponge laid in the wound. In 1877 Busch (198) obtained total necrosis of bone in rabbits by passing an electrically charged wire through them. W. Koch (199) ligated the nutrient vessels or plugged them with emboli; Barnabo (200) removed a portion of periosteum aseptically, or applied x-rays. Some of these experiments, especially those of Busch, were planned to study both regeneration of the marrow after its destruction and its ability to produce bone (Rost (196)), (42), (198), (189). From the results it can be stated that marrow has the ability to regenerate completely, and in a few weeks after complete destruction, newly formed marrow will be present to the original amount and with little histological difference from the original.

By the injection of certain irritants (particularly paraffin oils) it can be shown that the marrow reacts by marked connective tissue production (Rost), in imitation of the clinical bone diseases such as *ostitis fibrosa* and others, which are characterized by the replacement of marrow by connective tissue. In these, it is not certain if there is an irritant chemical involved, which varies with the different diseases, but produces a similar histological change. In the osteomyelitis of mother-of-pearl workers first described by Englisch (201), and later investigated roentgenologically, it is not improbable that the disease belongs to this group, and results from the action of conchiolin on the bone marrow. The circumstances surrounding the osteomyelitis of horn workers are less clear, but the writers regard this also as due to chemical irritation. In the latter disease there is an acute progressive suppurative osteomyelitis, but not called forth without the presence of infection. Experimentally, circumscribed abscesses were formed in which infection could be excluded with certainty by the injection of turpentine, mercury and certain other chemicals (202).

If an osteomyelitis develop in the vicinity of a joint, *i.e.*, in an epiphysis, the infection may spread and lead to a *suppurative arthritis*. Joints



have a very low resistance to infection, as found both clinically and experimentally. Magnus consistently obtained a typical joint infection in rabbits with 0.5 c.c. of an attenuated culture of staphylococci. Notzel believes that the synovial fluid is a good culture medium (203).

In man, infectious material may also reach a joint via the blood stream, or be introduced through direct injury.

The clinical picture of suppurative arthritis is usually that of a very severe infection with high fever and marked prostration. The danger of a generalized infection is by no means light. But it is not only the virulence of the organisms which causes the severity of the symptoms, but also the anatomical and physiological peculiarities of joints themselves.

A joint is a fairly homogeneous space, although in some, the knee for instance (204), certain subdivisions of practical importance may be made. Such a homogeneous space becomes infected rapidly and equally, and when pyogenic organisms are introduced, they are brought in contact with a large surface in a short time. This is equally true in chronic arthritides, something which is not often considered.

In clinical work, it is often observed that patients suffering from tuberculosis of some other organ, suddenly develop a painful transudation in a previously healthy knee joint, and the future course of events proves that it was the beginning of a tuberculous inflammation. The widely spread belief that the type of infective agent (gonococcus) can be diagnosed from the sudden onset of a markedly painful arthritis, is perhaps true, but with modifications.

This rapid swelling was also obtained in animals by Notzel, Dreyer, Magnus, Perez, and others.

But the rapid spread of bacteria cannot alone explain the severe general symptoms. The question is rather, are the bacteria and their toxins absorbed from a joint particularly fast and freely? This question has not as yet been answered satisfactorily (205). Studies of hemorrhages in joints had absorption as only a secondary interest. They have already been mentioned in the discussion of the fact that blood remains fluid in the abdominal cavity, and we refer to that paragraph. According to numerous anatomical investigations, the synovia are not in very intimate contact with lymph vessels, but as in all other parts of the body, the tissue fluids between the cells flow imperceptibly into the actual lymphatic system. Therefore, it is not possible to inject these vessels of the leg from within a joint (206), but their anatomical relations to those surrounding can be found in the investigations of Tillmann (207).

Braun, by injection of watery fluids, demonstrated a diffuse staining of the intracellular tissue of the synovia. The soluble part of the dyes was found later in the lymph nodes of the groin. The particulate elements



were phagocytosed by leucocytes which were then taken up in the circulation.

Absorption, however, occurs very slowly, according to the investigations of Braun. Cecca injected solutions of potassium iodide into joints and from the rate of its excretion in the urine, concluded that absorption begins in about 50 minutes. By massage, Mosengeil and Kroh hastened absorption, but damage to the synovia could not be excluded, as R. V. Volkmann pointed out. The latter is of the opinion that in injuries of the knee joint, blood is absorbed only at injured places by the tissues under the synovia, while the synovia itself hardly absorbs at all.

Daily clinical experience also shows that absorption from the inner surface of a joint is slow. Carbolic acid poisoning very rarely follows the injection of this substance into a joint. Effusions into the knee are absorbed very slowly, but inflammatory factors may play a role in this case. Viewed from the opposite standpoint, it is remarkable that increased joint fluid is not observed more often in severe general anasarca (cardiac decompensation, Braun), even if it does occur, according to Muller (208), more commonly than is supposed.

Notzel's experiments contradict these views. He discovered bacteria in internal organs in as short a time as five minutes after their injection into a joint. On the basis of his studies, he has advanced the rather startling view that the lymph nodes are not protective against infection, since, in his investigations, the bacteria passed through the lymph system so rapidly. His statements and conclusions, as might be expected, met with instant opposition (209). The first argument was that in injecting the bacteria, he introduced some directly into the blood stream. We know nothing definite, however, of the activity of the blood vascular system in absorption of joint effusions. In later experiments, Magnus could not confirm Notzel's findings.

To conclude, slow absorption is the very thing which does not explain the grave general symptoms. It is evident that further investigations are necessary.

The destructions of joints, well known in general pathological literature, as well as the contracture positions in effusions, have been studied in animals by many workers (210). Dreyer paid particular attention to the therapeutic measures in suppurative arthritis. In the treatment of joint diseases with effusion, therapeutic measures must be varied to suit the individual case. Temporarily disregarding the treatment of the infection, *per se*, stretching of the capsule is a danger which must be met by puncture because the synovia cannot absorb the fluid very rapidly and a flail joint may result. According to Payr, however, a certain amount of fluid is beneficial in preventing the excessive growth of connective tissue.

To prevent refilling, all sorts of irritant substances such as tincture of iodine, carbolic acid, etc. have been injected. According to Hildebrand (211), this refilling takes place because the nerve endings which surround the network of capillaries are stimulated from the inner layers of the synovia. These nerve endings are said to be concerned in the pouring out of the effusion, and Hildebrand believes that irritants reduce the abnormal sensitivity of the synovia and thus prevent the reaccumulation of fluid. This theory is not exhaustive for, of course, we see joint effusions in completely paralyzed limbs.

A further measure to prevent shrinking of the capsule and ligaments, consists in applying extension. There have been many investigations of the pressure relations during extension and of the force which must be exerted to separate joint surfaces (212). To these belong also the investigations of the tensile strength of the ligaments (213). The occurrence of so-called sprain fractures is a voucher for the fact that ligaments are often fastened tighter than bones.

These studies have shown that the application of extension apparatus reduces the pressure when the synovial membrane is normal; in a joint altered by inflammation or by effusion the opposite occurs, *i.e.*, a heightened pressure. But the results in the separate joints are varied. Why extension diminishes the pain is not entirely clear on these grounds, but possibly the changes in tension alone, even if the pressure is not reduced, are sufficient to modify the nerve endings.

*Tuberculosis of bones* like osteomyelitis is a blood borne infection. Experiments have established the interesting fact which can be used in the judgment of industrial accidents, that contrary to what occurs in osteomyelitis, the lodgement of tubercle bacilli in bone is not particularly favored by injury (214).

The peculiarities in the course of this disease can be explained by the type of infective organism and the body reaction to its invasion. In a general way, however, the considerations as outlined under osteomyelitis, apply to tuberculosis. The fact that tuberculous fistulæ heal with great difficulty, which leads us not to incise tuberculous abscesses, but puncture them, has been explained by Jochmann and Batzner (215) in the following way: in tuberculous inflammation, lymphocytes take part, and these contain no tryptic ferment such as is present in polymorphonuclear leucocytes; without this enzyme, the body is not able to dissolve the tuberculous tissue. Batzner, therefore, treated such fistulæ successfully with trypsin. It is doubtful though, if this hypothesis is correct. According to Rost (216), substances which stimulate granulation tissue are set free by the death of body cells, and it is quite conceivable that the injected trypsin acted favorably in this roundabout way. Furthermore, when mixed infection

is superadded, polymorphonuclear leucocytes containing trypsin are present in abundance and still the fistulæ do not heal. This question has not as yet been answered.

The mutual relationship between the muscular and skeletal systems which has been emphasized in this book becomes particularly clear after operative procedures on joints, particularly in their *artificial mobilization*. It is amazing to see how a new and useful joint develops even after complete removal of all the ligaments and parts of the capsule, together with a complete modification of the ends of the bones. The same laws and the same forces which interact at the first appearance of a joint in embryonal life, play a similar role in the final architecture of our operatively made joints. That the normal shape "in the strict sense of the word is fashioned by the muscles" was quite clearly realized by Ludwig Fick (11) as early as the year 1845.

In general, we seek to make from the ends of the bone a head similar to that found in the normal joint. It must be emphasized that this is the only correct way; the ball and socket are not developed just arbitrarily. In embryonal life, the end of the bone close to the insertion of muscles becomes the socket, and the end distant, the ball, as Rudolf Fick (11) expressed these laws of development. It is, therefore, the functions of muscles, pull, push and polish, which determine the future shape of the joint, and by changing the place of insertion of muscles, the shape and kind of joint can be modified.

After the ends of bones have been roughly shaped with chisel, saw and file, we place a piece of soft tissue between them to prevent union. This procedure was initiated by Helferich (217), who in 1894, implanted a piece of muscle while artificially mobilizing a joint, and thus gave this particular joint operation a tremendous impetus. It is possible to obtain a functioning joint without the interposition of soft parts, but the results of utilizing this suggestion of Helferich have been far superior. Numerous clinical and experimental studies have sought to discover other materials to place between the bone ends. Foderl, Roser, Chlumsky, Hubscher (218) used silver and gold foil, tin, celluloid, pig's bladder, etc. Narath, on the basis of the investigations of Foderl, once used a pig's bladder between the bones in a man. A fistula developed, but the final result was good. At the present time, because of better healing, tissue from the patient himself is used. Fascia, fat and periosteum have all been tried. American surgeons (Murphy (219)) usually use a soft part flap with a pedicle, while German surgeons prefer a free transplantation. Both methods seem to yield the same end results.

After a certain length of time, a capsular space appears between the ends of the bones and eventually contains a viscid, sticky fluid (220).



The bone ends themselves are covered with a tough connective tissue which has the gross appearance of cartilage and in a number of cases, this has been confirmed microscopically (221). This covering does not arise from the interposed material, indeed, the same lining develops without placing soft parts between, as was shown by Kocher and recently by Schmerz and Schepelmann (222).

The formation of the space has been studied experimentally, particularly by Rehn, and it was found that fatty tissue remains only along the edges, while the central part disappears, after undergoing a very typical metamorphosis (223). In the zone of degeneration cysts appear, and the final joint space is formed by their confluence. But Payr has a different idea. In his opinion, the principal factor is trauma, which acting as in the development of bursæ, in hallux valgus, finally leads to the formation of cysts. Payr relates the formation of the joint space to the cyst formation in ganglia, on which subject he had earlier made extended histological studies (224). But in this he is opposed by Ledderhose (225) who regarded the spaces in ganglia as true cystic tumors. At present, we cannot answer the question of how cysts filled with clear fluid develop in the tissues. It may be mentioned, however, that such cysts develop in parts of the body which have nothing to do with preformed bursæ, as for example, the hygromata derived from unusual bursæ in the popliteal space (221), which Langemak (226) believes, on the basis of his extensive histological studies of this subject, develop from fatty tissue. He observed a smooth transformation of fat to connective tissue, which later became a thickening composed only of collagen practically bloodless in the centre. Softening now took place and the collagen was changed to fibrinoid and albuminoid. The increase of fluid in such hygromata is, therefore, not an exudative process, but only a dissolving of collagen fibres. This would hold true for the space formation in artificially mobilized joints in which Salkowsky found "synovin" (227).

The normal synovial fluid is said to be a decomposition product and not a real secretion, but this view is doubted by Rudolph Fick (11). According to Bier (221) the synovial fluid contains ferments, which dissolve certain tissues, particularly bone. Therefore, when a peg of bone or ivory has been placed through the joint and the two bone ends in an arthrodesis, it is usually dissolved in a short time. Again, according to Bier, this property of bone tissue destruction also plays a role in the regeneration of joints.

The composition of synovial fluid varies according to whether the joint is quiet or in motion (80). It contains more water at rest; in motion, more solids, which are supposed to arise from decomposition products of the joint walls.



As mentioned above, ligaments and capsule develop in an artificially mobilized resected joint in almost the same relations as in the normal joint. The capsule is rebuilt from periarticular healthy tissue even when all fragments of the old capsule are carefully removed (Payr). It must be pictured here also that it is the performance of function which causes this adaptive change. But in this process there is an analogy to the development of capsule and ligaments in embryonal life (see R. Fick (11) p. 44), where it is also bound up with the function of the joint.

The dependency and relationship of the completed capsule to the musculature is seen again in the fact that pinching of the capsule during movements is prevented by the muscles. Furthermore, in anatomy, certain muscles are even called capsule tensors. But it is better perhaps to think of this stretching of the capsule as R. Fick does, *viz.*, that it is due to the tonus or the elasticity of the muscles and there is no actual "tensing" of the capsule.

That nature is able to rebuild a functioning joint with even much less help than is given by interposing soft parts and modelling bone ends, is shown in the classical treatise of v. Langenbeck (228) who not only observed a rebuilding of finger joints after subperiosteal resection, but also saw a whole new head of a humerus appear after resection. His work was based on Heine's animal experiments in subperiosteal resections, a work which was repeated by Ollier (229). Rebuilding of an elbow joint has been described by Jagetho and one of the hip by Schmieden (230).

In contrast to these simple resections are the experiments of implanting whole joints obtained by amputation or from cadavers (231). In this way, a new joint can also be obtained, but as learned from the pathological-anatomical investigations of Borst (232) and M. B. Schmidt on both human (cases of Enderlen) and animal material, these joints do not take on life, and thus are no different than the artificial ivory joints of König (233). These questions are so thoroughly discussed in general surgery that we need go no further into them here.

## VEINS

The veins of the body are subjected to a pressure, corresponding to the mass of blood which is supported vertically above the respective vessels (234). On account of the upright position of man, the highest pressure is exerted in the veins of the lower extremity. In adults, it amounts to 15 cm. mercury, it is therefore almost as great as the pressure in the aorta. As is well known, the walls of the veins are much weaker and less elastic than the walls of the aorta, and this pressure would, of course, stretch them to the breaking point if there were no special mechanism to support

it. The mechanism consists of the centripetally opening valves, and from the investigations of Delbert (235) we know that the pressure on the walls of the femoral vein is reduced from 15 to 1 cm. mercury by their presence. They are able to withstand considerably more pressure; in the experiments of Lowenstein, those in the greater saphenous vein were still competent under 50 centimeters of mercury (236). But they are not entirely efficient, and the healing of wounds of the leg is much delayed by unfavorable circulatory conditions if the patient allows the lower extremity to hang, while if the patient lies down, the reparative processes are hastened since the hydrostatic pressure is reduced to zero.

The forward movement of the blood occurs according to the laws of communicating tubes, and that forced into the arteries by the heart shoves the blood column in the veins before it. This passive venous circulation is helped considerably by the action of the muscles which first compress the veins and then allow them to expand and thus pump the blood forward (237). On account of this lack of changing muscle function, occupations which require long motionless standing on one place, baking, washing, surgery, etc., are said to predispose to varicose veins. This pumping action of the muscles has been used therapeutically in the treatment of this condition. Thus Katzenstein (238) proposed to transplant the saphenous vein to a channel prepared in the sartorius muscle. Such veins, in which advanced secondary changes are present are not likely to recover completely after this operation, but Katzenstein always noted a subjective improvement. The patients had a sensation as though the leg had become lighter in weight.

As the chief cause in the development of dilated veins in the lower extremity, that is, for the formation of varices, the purely mechanical hydrostatic pressure has always been emphasized. Obstruction to the blood flow, from intraabdominal tumors or pregnancy, or collections of fat at the foramen ovale, or very many other things are said to be the immediate exciting causes. This on the whole, can certainly not be true, for these latter troubles occur in many individuals but only a few develop varices, and then we have seen above, that the valves in the veins can withstand a much greater rise of pressure without becoming incompetent if they are normal.

The fact that varices may be present at birth and may be hereditary makes it possible that the primary change is in the walls of the veins. Anatomical search for deficiencies has been made (239), but for purposes of discussion, the studies of normal veins as brought out in the work of Lowenstein (236) and others are more useful. Lowenstein believes that in "normal youthful individuals there are two different types of veins, those which possess particularly weak musculature at the sinuses, and

those in which the weakest musculature is at a place distal to the valves." The development of the various changes, *i.e.*, so-called sinusectasias and true varices, are said to depend on these anomalies.

Ledderhose (240) has called attention to the fact that the dilatation in varicose veins in the majority of cases is not proximal and central from the valves, but distal and toward the periphery, which cannot be brought into harmony with the opinion that varicose veins result from hydrostatic pressure. Hasebrok (241) explains this in a different way. He believes that the whole theory of hydrostatic pressure as a cause is incorrect, and that the dilatation is brought about by transmission of arterial pulsation. He showed in models that arterial waves spread directly not only to those veins lying in their immediate neighborhood, but also to those which, as the veins of the skin, are relatively distant from the arteries. Indeed, in the models there appeared and remained, localized dilatations distal to valves which had been introduced into the thin rubber tubes. That these observations may be applied to conditions in the human subject is shown by a number of facts. The most interesting, is Hasebrok's conception of the so-called Trendelenburg experiment, which (242), as is well known, consists in emptying the veins of the skin by stroking the leg and then compressing the saphenous vein below the groin. If the leg is lowered while the pressure is retained, the vein remains empty or fills very slowly from the periphery; but as soon as the pressure is released, the blood flows in very rapidly from above downward. This experiment shows the relation of incompetent valves to varicose veins. It must, however, be first discovered if the valves in the veins communicating between the saphenous and those lying deeply are competent. The fact that in incompetency of the valves of the tributary veins, Trendelenburg's operation of tying the saphenous vein gives poor results is explained by Hasebrok in this manner; that the arterial pulsation waves are transmitted particularly vigorously to the veins in the skin (superficial veins). Hypertrophy of the vessels is also said to result, a finding which previously had been thought due to the consequence or response of the veins to the increased hydrostatic pressure. These pulse waves act more energetically the more the outflow is checked, and in this way Hasebrok explains the development of varices in abdominal tumors, etc. Furthermore, the waves are increased when the blood flow is particularly large in amount, and this accounts, for example, for the isolated varices occasionally seen in the arms of heavy laborers. That an arterial pulse can be frequently seen in greatly filled veins and varices, had already been emphasized by Ledderhose.

Undoubtedly this theory is attractive, because so much in the pathology which remains hazy by the hydrostatic theory can be explained by

this. The mistake should not be made, however, of regarding the matter as settled. In outspoken varices, hydrostatic pressure plays a very large role. For the explanation of the beginning of varices, the arterial pulsation wave theory can be drawn upon to advantage. But we should never disregard the conception that weakness of the walls also plays a part, although it can only be said that definite dilatation may be present at birth, in the arm as well as the leg, and that varicose veins undoubtedly are present in certain families.

But weakness of the walls may furthermore be acquired. To this class belong the varices of syphilis, a subject with an extensive literature (243). In addition, injury may occur from other infectious diseases and toxemias, but our knowledge is much less certain. Some injuries are assumed to be due to certain metabolites, as for example, in pellagra, in chlorosis, or other general systemic diseases. In pregnancy also, according to the opinion of the majority of the authors, the varices are not due to passive congestion alone, but to some sort of toxin which perhaps is related to the internal secretory mechanism. Kushimura (244) advances the theory that all of these injuries, high blood pressure in addition, do not act directly but indirectly through the nervous system and the changes in the walls of veins result from alterations of tonus. Very likely the idea of a weakness of walls cannot be escaped, even with this theory. Lesser (245) considers varices production as a neoplastic growth.

Thrombosis very frequently occurs in these varicose veins, especially when the patients are compelled to lie abed on account of some other cause. The fundamentals of the morphology of thrombi are treated in general pathology and general surgery (246). For surgeons, the causes of the development of thrombosis are of decided importance, for post-operative disturbances from this cause, and sudden death from resulting emboli mar the results of many operations. It is necessary in considering the experimental studies in this subject to emphasize that coagula found in dead animals are often very difficult to distinguish with certainty, from ante-mortem thrombi. Post-mortem coagula often have the structure and surface markings which are regarded as characteristic of thrombi (247), in which the markings are the result of the movement of blood (Zahn). How much the surface markings of post-mortem clots are influenced by the agonal processes cannot always be determined at autopsy (246), (248). It is possible, perhaps, to produce the morphological structure of post-mortem clots experimentally (249), for example, when an animal is rapidly injected intravenously with collargol. The entire blood clots, but the heart continues to beat. Such agonal coagulation must be reckoned with, if false conclusions are to be avoided in experiment.



There is considerable similarity between the production of a thrombus and the usual coagulation, and a large number of the factors which lead to coagulation of blood outside the body are also important for coagulation in the living body. The first is a slowing of the rate of blood flow. In speaking of the experiments on the thrombus question, we will return to the fact that thrombi form only when this occurs. Secondly, the condition of the vessel walls plays a large role. We know of numerous physiological experiments and observations during blood transfusions, that coagulation is diminished if the vessel walls with which the blood comes in contact are made smooth with paraffin. Finally, the same enzymic and precipitation processes must operate as in coagulation in a test tube, and changes in the equilibrium of the composition of the blood favor the formation of clots.

The various experiments were directed toward all of these three factors, but the most comprehensive and clearest are those which took as their starting point changes in the rate of blood flow and injury to vessel walls. The experiments of Brucke (250) are fundamental; he found that the blood in ligated vessels remains fluid. If this were not true, the surgeon could scarcely sew a vessel and certainly organ transplantation would be impossible. Damage or destruction to the vessel wall initiates coagulation and the blood finds a "crystallization center" in the debris (246), (251). Just as good a crystallization center can be provided with any dead substance, *e.g.*, a silk string in the lumen of the vessel (252). The finer processes of this form of thrombosis were studied by microscopical observations on the omentum or web of living frogs, where it was found particularly in the experiments with ligation, that the blood flow was first slowed. Such delicate structures as the vessels in the omentum were damaged severely enough to cause thrombosis by even touching with any sort of chemical. The experiments of Huter, Schwalbe (253) and others are of great interest in abdominal surgery. Huter found that touching with ether led to thrombosis. The human omentum seems to be less sensitive, at least, nothing was heard of thrombosis in this structure when peritonitis was being treated by ether. Thrombosis is produced much more readily by the injection of all sorts of chemical irritants directly into the vessels. Zahn used Lugol's solution. To produce a shrinking of varices by thrombosis, Linser advises the use of bichloride of mercury injections and a method of treating hemorrhoids is based on the same viewpoint, *i.e.*, carbolic acid injections. Thermic influences act in the same way when they reach the vessel wall from without. Clinically, extensive thromboses are well known in burns and frost bite. Gangrene from cold, which was observed frequently during the war with predilection for mild cold, depends on such thromboses; in

burns also, thrombosis of the smaller vessels with later involvement of the larger vessels is very common. Experimental studies of the effect of heat were made in the rabbit's ear by Klebswelt (254), Eberth-Schimmelbusch and others, while Zahn and others studied cold. That the relation of vessel wall injury to the development of thrombi should not be pictured too mechanically is clear from the findings of Enderlen (255) and Borst on transplanted vessels. They found but insignificant scales of clot along the suture line in autoplasmic transplanted vessels; in homeoplastic transplants, it is true that the wall was destroyed, but there was no thrombosis (256). In heteroplastic transplants the walls were completely destroyed and obstructed by thrombi. It follows that the protection against coagulation offered by a healthy vessel wall is some sort of "vital specific one."

These experiments were comparatively simple and led to uniform results, but the nature of thrombosis is by no means explained by them. The majority of post-operative thromboses require for explanation the assumption of the additional factor of change in the composition of the blood. There are many investigations of this point. A number of chemical substances such as collargol, ether and chloroform, glycerin, pyrogallate, bichloride of mercury and others lead to coagulation on being injected intravenously (246), (249), (257). We know further that transfusion, particularly when foreign blood is used, predisposes to clot formation and this was the main reason that transfusion was deserted for the subcutaneous administration for a time (258). Serum injections are often followed by coagulation; the rabbit often reacts with thromboses to the injection of ox serum (259). This hypersensitiveness increases with successive doses, and in anaphylactic shock, which, as is known, is initiated by repeated injections of the same serum, thromboses in the lungs are of fairly common occurrence (see discussion of anaphylaxis, p. 289). As a cause for this coagulation, changes in the enzymic content of the blood have been suspected. Arguing from normal coagulation, the first thought is precipitation of fibrin ferment, and substances such as fibrin, blood or pressed tissue juice, pus, extracts of tumors, etc., have been injected intravenously with coagulation as a result (260). With a similar idea in mind, Volcker (261) recently attempted to produce thrombi by the intravenous injection of clotted blood from the same species. Obviously, these various experiments were actuated by clinical aims. Thus Volcker believed that broken up blood in an operative field might, by direct entrance into veins, lead to thrombosis and embolism. According to the investigations of v. Durings (262), an absorption of fibrin ferment may take place after crushing a hematoma, by which coagulation is favored. The majority of post-operative thrombi do not occur at the

operative site, but in the saphenous vein, especially when it is varicose. This is further evidence for the view that circulatory disturbances are predisposing factors, as has been mentioned above. The experiments of Wright (263), who obtained thrombi by the injection of the pressed juice of the testis only when the tissues were rich in carbon dioxide allows the significance of circulatory disturbances to appear in still another light.

Important works in which pus was introduced into the blood stream sought to show the influence of bacterial infections in thrombus production (264). It seems that we may expect thrombosis in a certain percentage of cases, after the injection of large numbers of streptococci, *B. diphtheria* and *B. typhosus*, but *B. coli* cause no thrombosis. Clots can be obtained with much more certainty by the injection of the products of bacterial metabolism (toxins), (even with those of *B. coli*), and it may be that the thrombi obtained by introducing bacteria around the vessels is brought about by a filtering through of their toxins. This latter condition was not found when streptococci were used, which agrees very well with clinical data. When the lodgement of bacteria is favored by a local slowing of the circulation, the intravenous injection of *B. coli* both living and dead, leads to local thrombosis, and perhaps post-operative thrombophlebitis may arise in man under these conditions. Investigations have also been made to determine if a "weakened condition" predisposes to thrombus formation, a point of importance in clinical work, but in animals made anemic by hemorrhage, Vaguez (265) obtained no thrombi.

Comparison of experimental results with clinical experience leads to the conclusion that bacteria and their metastatic implantation are of great significance in the development of thrombi. The question of whether blood coagula or aseptic broken down hematomata are predisposing causes will have to be settled by statistical studies. The view that pressure on the veins of the leg, *e.g.*, in Trendelenburg's position, brings about thrombosis, rests on insecure grounds. Trendelenburg (266) himself gives good evidence that such an origin is improbable.

Usually, organization tissue grows rapidly from the wall of the vessel into the thrombus. Clinically, it is usually considered that organization is complete in 21 days and the danger of loosening of the thrombus with embolism has disappeared; microscopically, the organization is completed much earlier. Embolism and its results have been discussed under diseases of the lungs.

The development of *leg ulcers* depends directly on varicose veins and their resultant passive congestion (234). After the skin has been damaged by thrombotic and lymphangitic processes, mild injuries, or long standing pressure, as in tight shoes, etc. are sufficient to lead to ulceration. This



view has the advantage of being simple, and is the one predominant at the present time, but whether it is correct in all cases is doubtful. Extensive ulcers are often present without corresponding varicose veins, and conversely, ulcers are often absent with marked varices. Verneuil calls attention to the fact that dilatation of deep veins is often present when the superficial ones appear normal. But all ulcers and wounds of the leg, even when varicose veins are not present, heal poorly when the patient is not at rest, an indication that the stasis which is present when the leg is allowed to hang retards the healing of all wounds. But whether this poor ability to heal which is present in normal persons as well, is only a consequence of the retarded circulation in the legs, or whether it is related to a different healing ability in different parts of the skin of the human body, cannot be answered at present. It does not seem to depend on a peculiarity of the arterial supply of the skin, for Spalteholtz (267) demonstrated only small differences in the density of the subpapillary network in the sole of the foot and the calf of the leg. It would be interesting to know if this same poor healing is found among Japanese and Orientals, who, because of their short stature and because they spend many hours of the day in a squatting position, suffer much less from varicose veins than Europeans. If passive congestion is to be placed in the foreground of causes, it is remarkable that in varices, the foot on which the highest blood column presses is almost never the seat of an *ulcus cruræ*. It is not clear why a leg ulcer should be found almost always from above the ankle to the middle of the leg. Of course, the pumping of the veins is particularly poor because most of the muscles become tendons in this situation.

From French sources the view has often been expressed that leg ulcers must have a nervous cause, and certain anatomical findings are used as evidence (268). These may be secondary, but the fact is always conspicuous that legs with ulcers are objectively cold and the subjective temperature and touch sensations are lowered. All of these things can, of course, be explained by the local findings and disturbed metabolism of the part. Therapeutically, nerve stretching has been advised.

When one of the larger vessels of an extremity is ligated, the blood flows rapidly through the so-called collaterals toward the periphery, and thus the nourishment is assured. From antiquity, investigations have been made concerning the details of the development of this *collateral circulation* (269). The critical time is during the first immediate adjustment, which Bier (182) describes as the "preliminary" collateral circulation, which will be discussed in a moment.

O. Weber (270), Marey, and others believed that the blood is dammed up towards the center, causing a rise in blood pressure, which mechanically



drives it into the part made anemic by the ligature. That there is a general increase of blood pressure of some duration was recently confirmed by Katzenstein (271), who found it in the collateral vessels also.

But it is questionable if this increase is significant in the production of collateral paths when small vessels are ligated, although it is doubtless true that pressure differences are set up (272). V. Recklinghausen and Nothnagel (273) lay great stress on its diminution in the anemic area, and Bier believes differences of pressure cause the fluids to flow into the network of blood vessels. But he has an opinion of his own when he believes that the anemic area has a "pulling" power, which sucks up the blood, as a sponge fills when it is placed in water. He was led to this conception principally through observation of the reactive hyperemia following the removal of an Esmarch's bandage. It is doubtful, however, if this latter reaction is analogous to the response of the capillaries after ligation. Katzenstein (274) justly emphasizes that when an Esmarch bandage is removed the conditions are similar to those in a canal when a lock is opened; an excess of water streams off and later the normal fall of the river bed is resumed. But the remark of Bier, that when vessels of medium size are ligated, the collateral circulation appears not merely according to the laws of pressure differences, but also according to the laws of flow in capillary tubes, is quite correct. He believes it is not only physical laws which determine the distribution of blood, but there is also a vital activity of the capillaries themselves, chiefly in the prevention of venous backflow. Obviously these phenomena are not clearly understood because we have little knowledge of the active part played by capillaries in the total vascular bed. The arteries supplying the intestine apparently have many collaterals, yet ligation is poorly tolerated and it may be that it is due to their inability to suck up blood. Bier believes that this "blood sense" of an organ runs parallel to its general sensitivity, and an organ which has no pain sense lacks also this pulling power (275).

The development of a collateral circulation, furthermore, is independent of the nervous system, at least, as far as it concerns a large nerve supplying an extremity. Those lying in the vessel walls were not taken into consideration in the experimental methods of these authors (Bier, Katzenstein and others). The influence of nerve stimulation on the peripheral blood pressure was investigated with the conclusions that certain considerations could be held regarding the nerve supply of an extremity in the development of collateral paths, but these experiments were so complicated that most writers believe they point to nothing definite (Bier, Katzenstein and others) (276).

The same rules are applicable when venous trunks are ligated; *viz.*, the development and activity of the collateral circulation is dependent not

merely on the anatomically demonstrable collateral paths, but also on the reaction of the organ to changes in its venous circulation (277). Thus, for example, ligation of the vena cava distal to the entrance of the renal vein is well borne, while ligation above leads to death even though the veins of the kidney have sufficient anastomoses with the vena azygos, etc. In the formation of venous collaterals, the primary rise of pressure is important in overcoming resistances. If the nutrition of an extremity is less endangered when both large artery and vein are ligated simultaneously is answered variously. This question has not been investigated sufficiently.

If, on account of arteriosclerosis, the circulation of an extremity is not adequate, the leg may be saved in certain favorable cases by shunting the arterial blood into the veins (278), since the valves do not completely prevent backflow. In animals, such anastomoses have been attempted, but in general the results have been unsuccessful (279), (256).

If an artery wall is punctured or a small wound communicates with the lumen, the blood burrows into the surrounding tissue, which may encapsulate it and lead to the formation of an *aneurysm*. What is known as an arteriovenous aneurysm arises when both artery and vein are ruptured and a communication develops between them. In either case, in addition to the usual subjective symptoms of pain and fatigue, there is the objective symptom of bruit, which, in arteriovenous aneurysm, may be heard over almost the entire extremity. As the investigations of Verth (280) have shown in the latter, quite considerable disturbances of the general circulation appear which show themselves in hypertrophy and dilatation of the heart, and reflex irritability of the heart and large vessels.

The explanation of this bruit has led to much discussion (281). Franz anastomosed arteries and veins and studied the advent and disappearance of vessel sounds under experimental conditions which were similar to those occurring naturally. He found that there first arose a continual roaring sound which became discontinuous and changed its character when the vein was ligated toward the heart, while tying the peripheral end had no influence. It seems clear, therefore, that the sounds in an arteriovenous aneurysm arise in the vein and not in the artery and that they are related to the well known venous hum. Furthermore, it may be said from these researches, that the presence of bruit is not due to the clashing together of arterial and venous blood, as Billroth, among others, thought.

The old investigations of Th. Weber (282) which are now used in the explanation of the murmurs of endocarditis, apply as well to these bruits. If a glass tube is connected to a faucet and water allowed to flow through, no sound is audible until the rate of flow has reached a certain degree when

roaring sounds are heard. In aneurysms, we may assume that the increased rate of flow in the veins produces the roaring sounds. Other factors which probably contribute are vibrations of the wall of the vein and the above mentioned whirlpool at the narrow place of the anastomosis (von Bramann). According to Israel, such a venous murmur from increased rate of blood flow appears during every intravenous saline infusion if the fluid passes in under a certain pressure. The newer investigations of Muck have also shown that the venous murmur is related to this increased rate of flow.

In contrast to these venous noises we are led to consider the arterial murmurs. A sound is heard in an artery when a stethoscope is pressed against the vessel with sufficient force to narrow the lumen. Every surgeon is familiar with the peculiar scraping, intermittent character of the arterial murmur named after Wahl, which arises on cutting a larger artery. The scraping sound is increased during the arterial diastole (heart systole-Brugsch-Schittenhelm (283)). Since this sound arises only when an artery is opened, it is due in all probability to the change of flow of the blood mass from a narrow tube to a larger space. The bruit over soft goiter may be explained in a similar manner, that is, the change from narrow to wide in the arterial network. According to Bier (cited by Israel), the sound heard momentarily when an Esmarch bandage is removed, is due to the same cause.

The pain and the feeling of fatigue are due, no doubt, to pressure on neighboring nerves and to nutritional disturbances.

Without an external wound being manifest, a tearing of even large vessels may occur from all sorts of trauma. This has given occasion for the experimental examination of the elasticity of vessels, by which it was shown that the elasticity of both arteries and veins is very great, and exceptional circumstances are necessary to tear them (284). According to Botticher, the greatest danger is from sudden stretching. Even if the vessel is not completely severed, the intima may tear, roll up and thus partially obstruct the lumen.

Another very important possibility of vessel destruction must still be mentioned. If a foreign body, for instance, a drainage tube, is placed in the neighborhood of an artery (285), gradual erosion may occur. Cornelian, in 1843, discovered this fact in animals, and later Beyme (286) published clinical observations of such cases.

When small vessels are torn subcutaneously, we obtain what every layman knows as a "black and blue mark." Eschweiler (287) subjected this phenomenon to experiment and found that the "black and blue mark" arises only when the blood is present not deeper than 1 to 1.5 mm. under the skin. The color is derived from blood pigments, and it makes little



difference whether the blood is arterial or venous, but it is dependent to a considerable degree on the thickness of the hemorrhagic infiltration.

The *diseases of the lymphatics* are closely related to disturbances of the blood circulatory system. Both serve to convey to the cells the nutrition on which depends all those functions which we identify with life (206).

According to the present day viewpoint, the lymph in its vessels comes from the tissue fluids which bathe the individual cells, and is a product of both the substances in the blood capillaries and those produced by cell metabolism. How this fluid reaches the lymphatic channels is a question much discussed, but one which interests the surgeon but slightly. The flow of lymph is very slow, intrathoracic changes of pressure during respiration, contractions of muscles in the extremities, and of muscle fibres in the lymph vessels themselves, combine to force it onward. To this is added the pressure exerted by the newly formed tissue fluid and lymph (*vis a tergo*). This slow rate of flow is very effective in allowing the interchange of fluids between cells and lymph, and the lymph apparatus may be looked upon as our immediate organ of nutrition. Since this fluid reaches the individual cells, it is obvious that an endless number of injurious substances may reach them through this medium. They may be metabolic products, toxins of all sorts, and particularly bacteria.

Our knowledge of the part played by the lymphatic system in the struggle with bacteria, is quite extensive (288). According to Halban, the lymph nodes comprise a particularly valuable defense against invading organisms, which they hold purely mechanically, as if they were soot or pigment granules. They might be called filters in the line of the lymph flow. The length of time the organisms are held in the nodes, according to Halban, depends on their virulence; non-pathogens pass through very quickly, and soon reach the internal organs, while on the other hand, pathogenic organisms are held back. There thus occurs a purposeful selection. The bacteria are not usually destroyed in these organs which are poor in antibodies, but their virulence is weakened in ways unknown in detail. If, in performing this service, the nodes are broken down by suppuration, scar tissue replaces their parenchyma and they are ultimately entirely changed in structure.

It is a very pertinent question if new ones appear at the site of such a destroyed node, or of those removed operatively. According to experiment and observation, it seems fairly certain that they may be regenerated by budding from other nodes, or new ones may arise from fat tissue (289). That lymph channels also may be built anew has been known for a longer time. After amputation of the breast such regenerated lymph nodes may be felt in the fat as small nodules.



Lymphedema, *i.e.*, insufficient emptying of tissue fluids and lymph from subcutaneous tissue, is quite common (290). It is in this condition especially, that the close relationship between the blood and lymph vascular systems is brought out. Edema cannot be explained solely as an obstruction of lymph channels, as we will mention more definitely in speaking of elephantiasis, for experiments show that even after extensive removal of lymph nodes, stasis of lymph does not necessarily occur (289), (291). Clinical observations agree with this, provided that a complicating wound infection does not set in, or that the main trunk, the thoracic duct, is not ligated. In the latter case, marked dilatation of lymph channels occurs, especially those of the abdomen, although experimental results are not always consistent, because of anatomical anomalies, and the presence of collateral paths.

A disease in which lymph stasis is the prominent clinical feature is elephantiasis which is at present regarded as caused by obstruction to lymph drainage, usually from an inflammatory process. In Arabian elephantiasis, an infection of the lymphatic vessels with *filaria Bancrofti* (292) leads to the enormous swellings of the legs and scrotum. Elephantiasis graecorum is a particular form of lepra infection (293). The pathological physiological factors in that seen in our latitudes are most evident in cases in which the lymph nodes of the groin have been extirpated, or where carcinoma has invaded those of the arm, as in carcinoma of the breast. It has not been satisfactorily determined if stasis from destruction of the lymph nodes will fully explain the production of the colossal swellings, or if, as Carle and Jambon (294) believe, there must be added a lymphangitis. The fact remains, that we see a fairly uniform dilatation of all the lymph channels of the affected limb, with later fibrous thickenings and increases of connective tissue. It is exceedingly difficult to determine how much of this change is secondary (295). Undoubtedly, inflammations, especially those of an erysipelatous nature which pathologically anatomically are inflammations of the smallest lymph channels, do occasionally lead to an elephantiasis. Edematous swelling of a limb in infections, *e.g.*, the hand in phlegmons, is, of course, an every day surgical occurrence, but it is of shorter duration, and the secondary changes such as take place in elephantiasis do not occur. It is not difficult to understand that tuberculous and syphilitic inflammations, as well as blunt traumata (Rydygier) which destroy lymph channels, should bring about an elephantiasis, or that cardiac disease or nephritis may produce this condition permanently. The edema in syringomyelia is entirely unexplained (Remak); it may be due in part to the frequent phlegmons which arise in this disease (296).

But it is difficult to understand the elephantiac swelling of the leg in

those cases in which there is no demonstrable obstruction or destruction of lymph vessels. In the congenital type, it may be assumed that the amniotic band led to an interruption of lymph channels (297). But there still remain the so-called sporadic cases occurring mostly in young individuals, in whom, without any known cause, a slowly developing and increasing swelling of the leg appears. Whether we must assume here, as in varices, an unknown cause of the dilatation, or whether there is an obstruction in the groin is as yet not known. It is important in the treatment to know if the deeper lymph channels, *i.e.*, those in the muscles and bones, are also diseased, since attempts to give relief have been made by anastomosing the superficial with the deep channels, for example, by removing the muscle fascia (298). Unfortunately our knowledge of the pathological physiological occurrences in elephantiasis has not been enriched by the results of such procedures. Based on the view that the production of lymph is dependent on arterial supply, Carnochan (299) advised ligation of the femoral or iliac artery. This has been tried frequently but the results were poor, possibly because the disease had progressed too far. The rationale of the operation seems correct, even if the actual etiology of the disease is not taken into consideration. The results of excision of wedged shaped pieces from the skin are due to the interruption of the blood circulation, and in a similar way, the ligation of the saphenous vein in varices, to the interruption of the lymph channels (300).

Giantism and clubbed fingers are related superficially to elephantiasis (301). It has already been mentioned that clubbed fingers develop particularly in chronic suppurative lung diseases, and in cardiac lesions, but may be found also in all sorts of other conditions, such as liver diseases, or unilaterally, in aneurysms of the subclavian artery. How far their etiology may be regarded from a single viewpoint is at present not clear. Most authors believe clubbed fingers are only a symptom of an hypertrophy of various parts of the body, thus, the face especially is said to show a thickening (302).

Clubbed fingers are considered closely related to the hypertrophic osteoarthropathy of Pierre Marie (*v. Hoffmann* (303)). But knowledge of the etiology of this latter disease is also very hazy at present. The publications of Braun (304) are interesting, inasmuch as he found changes in the hypophysis in three cases from which it might be assumed that clubbed fingers have something to do with acromegaly. It remains, of course, an open question how these changes in the hypophysis were produced, and how they are related to the primary condition, *i.e.*, the disease in the lungs. Bamberger (305) offers the opinion that certain toxic substances are absorbed from the lung abscesses and these lead to

giantism. His experiments however, in which he administered to rabbits by rectum, the sputum from bronchiectatic cavities to obtain an increase in size of the extremities, similar to clubbed fingers, yielded only negative results.

#### LITERATURE TO EXTREMITIES

1. Roux: "Terminologie der Entwicklungsmechanik," Engelmann, Leipzig, 1912, p. 227.
2. Matti: "Die Knochenbrüche u. ihre Behandlung," Springer, 1918, p. 29.
3. Luciani: Human Physiol., 3rd. Vol., Chapter I, Macmillan Trans., F. Welby.
4. Grunewald: Ztschrft. f. orthop. Chir., 1919, 39.
5. Lit. see Fick: Handbuch d. Anat. u. Mechanik d. Gelenke, 2, p. 247 and Handbuch der Anat. des Menschen v. Bardeleben.
6. E. Weber: Mechanik d. menschl. Werkzeuge, Gottingen, 1836.
7. Aeby: Deutsche Ztschr. f. Chir., V. 6.
8. Hagenbach-Burckhardt: Ztschr. f. Orthop. Chir., 1907, 18, 358.
9. Bing: Med. Klinik., 1907, No. 1.
10. v. Meyer, H.: "Die Statik u. Mechanik. d. menschl. Knochengerüsts," Leipzig, 1873. Wolff, J.: "Die innere Architektur d. Knochen," Berlin, 1870; "Ueber die Wechselbeziehungen," zwischen d. Form. u. Funktion, Leipzig, 1901; Ztschrft. f. Orthop. Chir., V. 2.
11. Fick, R.: Handbuch d. Anat. des Menschen, 2-1-p. 43.
12. Ghillini: Arch. f. klin. Chir., V. 52. Hueter: Arch. f. klin. Chir., V. 2 and 9. Korteweg: Ztschrft. f. Orthop. Chir., V. 2. Wolff: L. C. Wien. klin. Wchschrft., 1893; Ztschrft. f. orthop. Chir., V. 2. Lorenz: Wiener klin. Wchschrft., 1893, No. 9, 10, 11. v. Volkmann: Krankheit d. Bewegungsorganen in Pitha-Billroth's Handb., V. 2; Virchows Arch., V. 22.
13. Fick, R. and Strasser: Lehrbuch d. Muskeln, Gelenkmechanik, 3 vols. Springer.
14. Fuld: "Experimental proof," Arch. f. Entwicklungsmechanik, 1901, V. 11.
15. Braus: Morphol. Jahrbuch., 1906, V. 35.
16. Fick and Gabler: Molerschotts Unters. z. Naturlehre, 1860. Joachimsthal: Ztschrft. f. orthop. Chir., 1896, V. 4, p. 169; Arch. f. klin. Chir., Vol. 54. Marey: Arch. de physiol. norm. et pathol., 1889; Compt. rend. hebdomadaire des seances de l'acad. des sci., 1887. Weber, E. F.: Verh. d. sachs. ges. d. Wissensch. Math. phys., Kl., 1867.
17. Bethe and Parnas: Allg. Anat. and Physiol. d. Nerven systems, 1903.
18. v. Uexküll: "Umwelt und Innenwelt der Tiere," 1909, p. 91.
19. Boeke: Anatom. Anzeig., 1910, V. 35; 1913, V. 44.
20. Frank: Berlin. klin. Wchschrft., 1919, No. 45.
21. Mosso: Arch. Ital. de Biol., 1904, 41.
22. Weiss: "Die Muskelarbeit nach d. Untersuchungen von Chauveau," Ergeb. d. Physiol., 1910, 9, 370.
23. see Zuppinger Christen: Allg. Lehre von den Knochenbrüchen.
24. Du Bois-Reymond: Spezielle Muskelphysiologie, Berlin, 1903; Nagel's Handbuch der Physiol., V. 4, p. 601.
25. Fischer, O.: Ztschrft. f. orthop. Chir., 1908, V. 22 (summary).
26. v. Bayer: Natur. hist. med. Verein. Heidelberg, 1919.
27. Heuter: Virch. Arch., V. 28 and 46. Henke: Ztschrft. f. rat. Med., V. 33, p. 141.
28. Purkhauer: Ztschrft. f. orthop. Chir., V. 21, p. 174.

29. Becker: Inaug. Dias. Wurzburg, 1917.
30. v. Frey: Sitz. Ber. bayr. Akad. d. Wissensch. math. physik. Klasse, 1912.
31. Lehmann: Munch. med. Wchschrft., 1916.
32. v. Frey: Sitzungsber. der physik med. Gesell. Wurzburg, 1917. Payr: Deutsch. Ztschr. f. Chir., V. 129, p. 356.
33. Wundt: Vorlesungen über die Menschen u. Tierseele, 6th Edit., Vass. Leipsig, 1919.
34. Vanghetti-Sauerbruch: Brun's Beitr., V. 98, p. 761.
35. Kron: Deutsch. med. Wchschrft., 1910, No. 47.
36. Reich: Habilitationsschrift, Tübingen, 1910.
37. Gobel: Deutsch. Ztschrft. f. Chir., 1913, 122. Gluck: Arch. f. klin. Chir., V. 26. Hildebrandt: Archiv. f. klin. Chir., 78. Helferich: Arch. f. klin. Chir., V. 28. Wrede: Chirurgencongress, 1912. Haberland: Inaug. diss. Leipsig, 1913. Eden: Arch. f. klin. Chir., 111, Muskeltransplantation in Lexer Die freien Transplant Neue Deutsch. Chir., 26 a. Volkmann: Ziegler's Beiträge, 1893. Erlacher: Arch. f. klin. Chir., 106. Magnus: Munch. med. Wchschrft., 1913. Landois: Mitt. a.d. Grenzgebiet u. Kuttner; Chirurgie der quergestreiften Muskulatur., Deutsche, Chir., 25, 1.
38. Zenker: "Über die Regeneration des quergestreiften Muskelgewebe," Leipsig, 1864.
39. Kuttner and Landois: Chir. d. Quergestreiften Muskulatur Neue deutsch. Chir., 25 a. 13.
40. Bier: Deutsch. med. Wchschrft., 1918, No. 34.
41. Marchand: "Der Process der Wundheilung," Deutsche Chir., No. 16.
42. Haab: Untersuch. a.d. pathol. Inst. Zurich, 1875, 3. Bidder: Arch. f. klin. Chir., V. 78; Zentralbl. f. Chir., 1876. Bier: Deutsch. Med. Wchschrft., 1918. Bajardi: Moleschott-Unters. z. Naturlehre, 1882, V. 13. Maas: Arch. f. klin. Chir., 1872, V. 20. Ollier: "Regeneration des os," Paris, 1867, V. 1, p. 111 etc. partic. p. 150. Martin: Arch. f. klin. Chir., V. 113, p. 1. Hilty: Ztschrft. f. rat. med., 1853, V. 3.
43. Franke: Berlin. klin. Wchschrft., 1917. Schmidt, G. B.: Naturhist-med. Verein Heidelberg, 1917; disc. of paper by Franke.
44. Dax: Bruns Beit., V. 104, p. 313.
45. Damascelli: Arch. f. klin. Chir., V. 58. Kapsammer: Arch. f. klin. Chir., V. 56.
46. Bloch: Revue de Chirur., 1900. Lennander: Deutsch. Ztschrft. f. Chir., V. 73. Grenzgebiet, 1906, V. 15. Nystrom: Deutsch. Ztschrft. f. Chir., 1917, 142.
47. Piorry: Dict. des sciences med. T. 51, Art. Sensibilite, Paris, 1821.
48. Fick: Handbuch d. Anat. d. Menschen. Von Bardeleben, 2, p. 20.
49. Sudeck: Deutsch. Chir., 1913, 25 a. p., 137.
50. Grunewald: Ztschrft. f. orthop. Chir., 1912, 30.
51. See Lange: Ueber funk. Anpassung, etc., Springer, 1917.
52. Horvart: Ueber Hypert. d. Herzens, Wien, 1898.
54. Teleky: Wiener klin. Wchschrft.
55. Furnrohr: Munch. med. Wchschrft., 1907.
56. Nothnagel: Ztschrft. f. klin. Med., V. 10. Tillmann: Arch. f. klin. Chir., V. 69. Zenker: Berlin klin. Wchschrft., 1883. Kremer: Inaug. Dissert. Greifswald, 1902.
57. Burn: Naturforscherversamm. Meram, 1905. Bumm: Wiener. med. Presse, 1906. Brandes: Chirurgencongress, 1913. Sulzer: Festschrft. f. Ed. Hagenbach, 1897. Grossmann: Wiener klin. Wchschrft., 1912. Schiff and Zack: Wien. klin. Wchschrft., 1912. Legg: Am. J. Orthop. Surg., 1908.



58. Krauss: Virch. Archiv., V. 113.
59. See Strasser: Lehrbuch d. Muskel u. Gelenk mechanik, 1908, V. 1, p. 136, Springer.
60. Heidenhain: Munch. med. Wchscrft., 1915.
61. Lovett: Ztschrft. f. orthop. Chir., 1913, V. 32 (lit.).
62. Strumpell: Vulpian Munch. med. Wchscrft., 1888.
63. Hoffa: v. Volkmann's Sammlung klin. Vortrage, N.F., No. 50. Deroche: These de Paris, 1890. Charcot: Maladies du systeme perveux, V. 3. Lecons sur l'appareil vasomoteur, 1875, V. 2. Raymond: Revue de Med., 1890, p. 374.
64. Klippel: Bull. d. la. soc. anat., 1888.
65. Vazin: Cited by Heidenhain, Monatsschrft. f. Unfallheilkunde, 1894, V. 1.
66. Frey: Nagels Handbuch der Physiologie.
67. Mosso: Arch. ital. de Biol., V. 25.
68. Brandes: Fortschritte auf. d. Gebiet. d. Rontgenstrahlen, V. 21. Sudeck: Arch. f. klin. Chir., V. 62, p. 147 and l. c. Kienbock: Wiener med. Wochenschrft., 1901.
69. Wolff: Berlin klin. Wchenschrft., 1883-1888. Arch. f. klin. Chir., V. 20.
70. Volkmann: Virchows Archiv., V. 24, p. 512. Konig: Arch. f. klin. Chir., V. 9, p. 193.
71. Bardenheuer: See Steinmann, Lehrbuch d. funkt. Behandlung d. Knochenbruche, Stuttgart, 1919, Enke, p. 40.
72. See Oppenheim: Lehrbuch der Nervenkrankheiten, 5th Edition, V. 1, p. 462.
73. Jamen: Lehre von der Atrophie Gelahmter Muskeln, Jena, 1904, Fischers Verlag.
74. Perthes: Munchener Med. Wochenschrft., 1919, V. 1017.
75. Stier: Arch. f. Physiol., 1897, V. 29. Vulpian: Arch. de physiol., 1869, V. 2.
76. Gayet and Bonnet: Coll. ref. Arch. gen. de Med., 1901.
77. Regnier: Monatsschrift f. Unfallheilkunde, 1901.
78. Menzels: Arch. f. klin. Chir., V. 12.
79. Reyher: Deutsche Ztschrft. f. Chir., 1873, V. 3. Moll: Virchows Archiv., 1886, V. 105.
80. Hildebrand: Arch. f. klin. Chir., V. 81, p. 418.
81. v. Volkmann: Berlin. klin. Wchenschrft., 1870.
82. Bauer: Konstitutionelle Disposition zu inneren Krankheiten Springer's Verlag., 1917, p. 33.
83. Grawitz: Arch. f. klin. Chir., V. 111.
84. Bussmann: Die path.-hist. Erklarung zu Bader u. Massagegwirkung bei versteiften Gelenken Greifswald, 1919, 1. D.
85. Riedinger: Handbuch d. orthop. Chir., 1, p. 143.
86. Bonnet: Traite des maladies des articulation, Paris, 1845.
87. A. Fick: Die Medizinische Physik., Braunschweig, 1885.
88. Konig: Zentralbl. f. Chir., 1893, V. 52.
89. Bahr: Monatsschrft. Unfallheilkunde, 1895, V. 2, p. 322.
90. Lucke: Deutsche Ztschrift. f. Chir., 1885, V. 21.
91. Weber: Mechanik. d. Menschl. Gehwerkzeuge.
92. Hildebrand: Ztschrft. f. Arztl Fortbildung, 1910.
93. Schanz: Zentralbl. f. Chir., 1914.
94. Forster: Ztschrft. f. orthopad. Chir., V. 36, p. 304. Coenen: Arch. f. Orthopadie, V. 15. Jansen: Ztschrft. f. Orthopad. Chir., 1915, V. 35.
95. Herz: Ztschrft. f. orthopad. Chir., 1910, V. 25.
96. Strasser: Lehrbuch d. Muskel-u. Gelenkmechanik. Verlag. v. Springer, Berlin, 1919.

97. Heidenhain: *Monatsschrift f. Unfallheilkunde*, 1894, V. 1.
98. Fischer: *Deutsche Ztschrft. f. Chir.*, V. 8, p. 1.
99. Jansen: *Ztschrft. f. orthopad. Chir.*, 1914, p. 34.
100. Ritters: *Beitr. zur naheren Kenntniss des Galvanismus usw.*; Jena, 1802.
101. Grunewald: *Ztschrft. f. orthopad. Chir.*, V. 30, p. 14.
102. Lorenz: *Wiener med. Wochenschrft.*, 1910.
103. Kimura: *Zieglers Beitr.*, 1900, V. 27. Weichselbaum: *Virchows Arch.*, 1872-V. 55. Roser: *Arch. f. physiol. Heilkunde*, 1856. Anhausen: *Charité' Annalen*, 1909, V. 33. *Arch. f. klin. Chir.*, V. 94, 99, and 104. *Deutsche Ztschrft. f. Chir.*, 110, Berlin. *klin. Wchenschrft.*, 1913 and 1915. R. Beneke: *Festschrift d. 69 Vers. d. Naturf. u. Ärzte Braunschweig*, 1897. Walkhoff: *Verh. d. deutsch. Pathol. gessel Meran*, 1905. Pommer: *Denkschrft. d. kais. Akademie der Wissenschaften*, 1914, v. 89, p. 65. Wollenburg: *Festschrift. f. orthopad. Chir.*, 1909, V. 24 and 26. *Arch. f. orthopad.*, 1908, V. 7. Ziegler: *Lehrbuch der spez. pathol. Anat.*, 1887, 5th Edition. v. Volkmann: *Pitha-Billbroth, Handbuch, d. allg. u. spez. Chir.*, Vol. 2.
104. Magnus: *Arch. f. klin. Chir.*, V. 102. Tashiro: *Ziegler's Beitr.*, 1903, V. 34.
105. Gies: *Deutsche Ztschrft. f. Chir.*, V. 18, p. 8.
106. Stempel: *Deutsche Ztschrft. f. Chir.*, V. 60.
107. Preiser: *Ztschrft. f. orthopad. Chir.*, V. 26; 80 *Naturforscherversammlung*, Kohn, 1908; *Statische Gelenkerkrankungen*, Stuttgart, 1911.
108. Walkhoff, Ewald and Preiser: *Ztschrft. f. orthopad. Chir.*, 1911, V. 28. Axhausen and Pels: *Deutsche Ztschrft. f. Chir.*, V. 110.
109. Preiser: *Deutsche Ztschrft. f. Chir.*, V. 89.
110. Kroh: *Deutsche Ztschrft. f. Chir.*, V. 99.
111. König: *Arch. f. klin. Chir.*, V. 88.
112. Lesshaft: *Anat. Anzeiger*, V. 1, p. 120.
113. Lane: *Lancet*, 1889.
114. Hoffa: *Handbuch der. prakt. Chir.*, V. 4, p. 569.
115. Weichselbaum: "Die senilen Veränderungen der Gelenke," *Kais. Acad. d. Wissensch. Wien*, 1877, v. 75.
116. Monro: cited by Barth, *Arch. f. klin. Chir.*, V. 56, p. 509.
117. König: *Deutsche Ztschrft. f. Chir.*, 1888, V. 27, p. 90.
118. Budinger: *Deutsche Ztschrft. f. Chir.*, 1906, V. 84.
119. Poncet: *Revue de Chir.*, 1882, V. 2. Kragelund: *Zentralbl. f. Chir.*, 1887.
120. Barth: *Arch. f. klin. Chir.*, V. 56. Rimann: *Virch. Archiv.*, V. 180. Hildebrand: *Deutsche Ztschrft. f. Chir.*, V. 42, p. 292. Cornil and Condray: *Revue de Chir.*, 1905. Gies: *Deutsche Ztschrft. f. Chir.*, V. 16, p. 337.
121. Bier: *Deutsche med. Wchenschrft.*, 1919.
122. Seggel: *Deutsche Ztschrft. f. Chir.*, V. 75.
123. Martens: *Deutsche Ztschrft. f. Chir.*, V. 53, p. 348 and 485.
124. Kragelund: *Zentralblatt f. Chir.*, 1887, p. 412. König: *Deutsche Ztschrft. f. Chir.*, 1888, V. 27; *Zentralbl. f. Chir.*, 1905. Paget: *St. Barthol. Hosp. Reports*, V. 6. Broca: *Denkschrift z. Feier d. 10 Jahr Stiftungsfestes d. Vereins deutscher Ärzte in Paris*, 1854.
125. Klein: *Virchows Archiv.*, 1854, V. 29, p. 190.
126. Ludloff: *Arch. f. klin. Chir.*, V. 87.
127. Hildebrand, Scholz and Wieting: "Das Arteriensystem d. Menschen im Stereoskopischen Röntgenbild Wiesbaden, 1904.
128. Kirschner: *Arch. f. klin. Chir.*, V. 104.

129. Hahn: Arch. f. klin. Chir., V. 104. Fischer: Deutsche Ztschrft. f. Chir., V. 12.
130. Schmieden: Arch. f. klin. Chir., 1900, V. 62, p. 542. Real: Deutsche Ztschrft. f. Chir., 1894, V. 38.
131. Kraske: Zentralbl. f. Chir., 1879; Enp. Untersuch. über d. Regeneration querge-steifter Muskelfasern, Halle, 1878. Leser: v. Volkmann's Sammlung klin. Vortr., 1884. Heidelberg: Arch. f. exp. Path. and Pharm., 8. v. Volkmann: Zentralbl. f. Chir., 1881.
132. Bardenheuer: Deutsche Ztschrft. f. Chir., 108.
133. Kroh: Deutsche Ztschrft. f. Chir., 1913, V. 120.
134. Rost: Munchener med. Wchenschrft., 1916, V. 2.
135. Hildebrand: Deutsche med. Wchenschrft., 1905, p. 1577; Samml. klin. Vortrage, 1906.
136. Hildebrand: Deutsche Ztschrft. f. Chir., V. 45, p. 584. Mikulicz: Zentralbl. f. Chir., 1895.
137. Voelcker: Bruns. Beitr., V. 33; Handbuch d. prakt. Chir., 1913, V. 2, 4th Edition.
138. Schloessman: Bruns Beitr., V. 71, p. 209.
139. Blenkle: Arch. f. klin. Chir., V. 103. Jungling: Bruns Beitr. z. klin. Chir., V. 78. Stempel: Mitt. a.d. Grenzgeb., V. 3. Trappe: Fortschr. a.d. Gebiete d. Rontgenstrahlen, 1897, V. 11. Goto: Arch. f. klin. Chir., V. 100. Frattin: Fortschritte a.d. Geb. d. Rontgenstrahlen, V. 19.
140. Kuttner for lit. Ergebn. d. Chir., 1910, V. 1. Sudeck: Deutsche Ztschrft. f. Chir., 1919, V. 150, p. 107.
141. Ropke: Arch. f. klin. Chir., 1907, V. 82.
142. Brunner: Handbuch d. Wundbehandlg. Neue Deutsche Chir., 1916, No. 20, p. 92 and 93.
143. Voelcker: Naturhistorisch Medizinischer Verein, Heidelberg, 1915.
144. Sudeck: Deutsche Ztschrft. f. Chir., 1911, V. 108, p. 353.
145. Gruber: "Über Histologie u. Pathogenese der Zirkunskripten Muskelverknöcherung," Jena, 1913; Mitt. a.d. Grenz., 1914, V. 27; Bruns Beitr., 1917, V. 106, p. 284. Pochhammer: Arch. f. klin. Chir., 1911, V. 94, p. 353.
146. Berthier: Arch. de med. exp., 1894, V. 6. Nakahara and Dilger: Bruns Beitr., V. 63. Malchol: Bruns Beitr., 1908, V. 56. König: Chirurgenkongress, 1906.
147. Kolb: Munchener Med. Wchenschrft., 1916, V. 29.
148. Delkeskamp: Fortschr. a. d. Gebiete, d. Rontgenstrahlen, V. 10.
149. Bier: Med. Klinik, 1905. Hildebrand: Med. Klinik., 1905.
150. Liek: Arch. f. klin. Chir., V. 80.
151. Wilms: Fortschr. a. d. Geb. d. Rontgenstrahlen, 1906, V. 3.
152. Borchard: Deutsche Ztschrft. f. Chir., 1904, V. 68 and 72. Kuttner: Berliner klin. Wchenschrft., 1908. Levi and Ludloff: Bruns Beitr., 1903, V. 63.
153. Steinert: Mitt. a. d. Grenzgeb., 1910, V. 21.
154. See Edinger: Orthopad. Kongress, 1916. Ztschrft. f. orthopad. Chir., 1917, V. 36.
155. Kruger: Munchen. med. Wchenschrft., 1916.
156. Bethé: Allg. Anat. and Physiol. d. Nervensystems, Leipzig, 1903, p. 182.
157. Hacker: Zentralblatt f. Chir., 1914, part 21. Erlanger: Zentralblatt f. Chir., 1914, pt. 15. Heinecke: Zentralbl. f. Chir., 1914, pt. 11.
158. Erlacher: Ztschrft. f. orthopad. Chir., 1914, V. 28 and 34.
159. Baus: "Die Entstehung der Nervenbahnen," Naturforschervesammlung Karlsruhe, 1911.
160. Rost: "Gesicht u. Mundhöhle" Borchard-Schmiedin, Lehrbuch d. Kriegschirurgie.

161. Boeke: Pflüger's Archiv., 1913, V. 151, p. 57.
162. Spitzzy: Ztschrft. f. orthopad. Chir., V. 13, 14, and 15.
163. Mayersbach: Ztschrft. f. orthopad. Chir., 1911, V. 28.
164. Stoffel: Ztschrft. f. orthopad. Chir., V. 25, p. 505.
165. Borchardt-Wjasmensku: Bruns Beitr., 1917, V. 107, p. 553.
166. Bethe: Deutsche med. Wchnschrft., 1916.
167. Stoffel: Ztschrft. f. orthopad. Chir., V. 38.
168. Schoppe: Lit. Zentralbl. f. d. Grenzgeb., 1915, V. 19; pt. 1 and 2.
169. Popper: Wiener klin. Wchnschrft., 1918, p. 1135. Schlossman: Ztschrft. f. d. ges. Neurol. u. Psychiatrie, 35.
170. Perthes: Munchener med. Wchnschrft., 1918, p. 1367.
171. Forster: Ztschrft. f. orthopad. Chir., V. 36, p. 318. Konen: Arch. f. Orthop., V. 15.
172. Renton: Brit. med. Journ., 1898. Quenin: 22 Franz. Chirurgenkongress, 1892. Bardenheuer: "Naturforscherversammlung," Harnburg, 1901. Partsch: Cited by Blessing, Ergeb. d. Path., V. 17.
173. Conrad: Diss. Greifswald, 1876. Kolliker: "Die Verletzungen u. Erkrankungen periph. Nerven," Deutsche Chir., 1890, V. 24. Stintzing: Ueber Nervendehnung, Leipzig, 1890. Vogt: "Die Nervendehnung als Operat. i. d. Chir. Praxis, Leipzig, 1877.
174. Hoffmann: Arch. f. klin. Chir., V. 69, p. 672.
175. Wilms: Fortschr. a. d. Gebiete d. Rontgenstrahlen, 1900, V. 3.
176. Volkmann: Chirurgenkongress, 1886. Zentralbl. f. Chir., 1882.
177. Charcot: Chirurgie des Maladies du systeme nerveux, Paris.
178. Cassirer: "Die trophischen Störungen" in Lewandowsky, Handbuch d. Neurologie.
179. Fuchs: "Lehrbuch der Augenheilkunde," 1907, 2 ed., p. 340.
180. Spiess: Munchener med. Wochenschrft., 1906, No. 8.
181. Breslauer: Deutsche Zeitschrft. f. Chir., 150.
182. Bier: Virchow's Arch., 1897 and 147. 1898, V. 153.
183. Bruce: Arch. f. exp. Pathol. and Pharmakol., 1910, 63.
184. Trendelenberg: Neurol. Zentralbl., 1906.
185. Boeckel: Gaz. med. Strazsbours, 1858 and 1869. Waldeyer and Volekmann: Cited by Lucke Deutsche Ztschrft. f. Chir., 1874, 4, 218. Demme: Arch. f. klin. Chir., 1862. Chassaignac: Gaz. med., 1854. Gosselin: Arch. gen. de. med., 1858. Roser: Arch. f. Heilkunde, 1865. Lucke: Deutsche Ztschrft. f. Chir., 1874, V. 4, p. 218.
186. Rosenbach: Deutsche Ztschrft. f. Chir., 1878, V. 10, p. 369 and 492.
187. Kocher: Deutsche Ztschrft. f. Chir., V. 10, p. 87 and 218.
188. Becker: Deutsche med. Wochenschrft., 1883, p. 664.
189. Becker: "Mikroorganismen bei Wundinfektionskrankheiten des Menschen," Wiesbaden, 1884. Rodet: Compt. rend. acad. d. sc. 1884, V. 99, p. 569. Courmont and Gabonlay: Compt. rend. de. Biol., 1890, V. 42, p. 186 and 274. Lexer: Arch. f. klin. Chir., V. 48, 52, 54. V. Volkmann's Samml. klin. Vortr., V. 173. Marwedel: Ziegler's Beitr., 1897, V. 22, p. 507. Enderlen: Deutsche Ztschrft. f. Chir., 1899, V. 52, p. 293 and 507. Lannelogne: Annal de l'inst. Past., V. 5, p. 209.
190. Lexer, Kuliga and Turk: "Untersuchungen über Knocharterien," Berlin, 1904, Aug. Hirschwald.
191. Biers: Hyperämie als Heilmittel. F. C. W. Vogels Verlag.



192. Samuel: Virchows Archiv., V. 127. Roger: Compt. rend. de Soc. de Biol., 1890.
193. E. Fraenkel: Mitt. a. d. Grenzgebieten, 1903, Nos. 11 and 12.
194. Buchner: Berlin klin. Wochenschrft., 1890. Romer: Virchow's Arch., V. 128. Pasteur: Bull. 1878. Leber: Lehre v. d. Entzündungen, Leipzig, 1891.
195. Kraus: Wiener klin. Wochenschrft., 1900. Kolle and Otto: Ztschrft. f. Hyg., V. 41. Coenen: Bruns Beitr., 1908, V. 60. Hormuth: Bruns Beitrage, V. 80. Flugge: Ztschrft. f. arztl. Fortbildung, 1910. Schultze: Ztschrft. f. Hyg., 1905, V. 50. Koch: 37 Chirurgenkongress, 1908, p. 220. Noguchi: Arch. f. klin. Chir., 1911, V. 96. Rost: Deutsche Ztschrft. f. Chir., V. 125, p. 126, with Saito. Neisser-Wechsberg: Ztschrft. f. Hyg., 1901, V. 36.
196. Rost: Deutsche Ztschrft. f. Chir., V. 125 and 127; Med. Klinik, 1914.
197. Hartmann: Virch. Arch., V. 8, p. 114.
198. Busch: Arch. f. klin. Chir., V. 20, p. 237; V. 22, p. 794.
199. W. Koch: Arch. f. klin. Chir., V. 23, p. 315.
200. Barnabo: Chir., Kongresszbl., V. 3, p. 241.
201. Englisch: Wiener med. Wchnschrft, 1870. Broca and Tridon: Revue de chir., 1903.
202. Enlenberg: Handbuch d. Gewerbehygiene, Berlin, 1876, p. 584. Grawitz and De Barry: Virchows Arch., V. 108. Councilmann: Virchows Archiv., V. 92. Gussenbauer: Arch. f. klin. Chir., 1875, V. 18. Grawitz: Virchow's Arch., V. 110. Rost: Deutsche Ztschrft. f. Chir., V. 125. Scheuerlen: Arch. f. klin. Chir., V. 32 and V. 36. Schmorl and Ingier: Frankfurter Ztschr. f. Pathol., 1913, V. 12; Pathologen Kongress, 1913. Klemperer: Zeitschrft. f. klin. med., V. 10. Orthmann: Virchow's Arch., V. 90. Uskoff: Virchow's Arch., V. 86.
203. Dreyer: Bruns Beitr., V. 75. Notzel: Arch. f. klin. Chir., V. 81. Magnus: Arch. f. klin. Chir., V. 102. Perez: Deutsche Ztschrft. fur Chir., V. 63.
204. Payr: Munchener med. Wchnschrft., 1915, No. 37-39.
205. Neuhaus-Hildebrand: Arch. f. klin. Chir., V. 81, p. 422. Cecca: La clin. Chir., 1907. Riedel: Deutsche Ztschrft. f. Chir., V. 12. Notzel: Arch. f. klin. Chir., V. 81. Kroh: Deutsche Ztschrft. f. Chir., V. 94, p. 215. Jaffe: Arch. f. klin. Chir., V. 54. Braun: Deutsche Ztschrft. f. Chir., V. 39. Mosengeil: Arch. f. klin. Chir., V. 19. Pagenstecher: Mitt. a. d. Grenzgebieten, 1912, V. 25. Tillmann: Arch. f. Mikrosk. Anat., V. 12.
206. Most: "Chir. d. Lymphgefasse," Neue Deutsche Chir., V. 24.
207. Tillman: Zentralbl. f. Chir., 1875 and Arch. f. mikrosk. Anat., 1876, V. 12, p. 679.
208. Muller: Deutsche Ztschrft. f. Chir., V. 100, p. 385.
209. Ribbert, Kruse, and B. Fischer: Niederhein. Ges. f. Natur-u. Heilkunde, Bonn, 1908.
210. Gies: Deutsche Ztschrft. f. Chir., V. 18, p. 8. Schablowsky: Arch. f. klin. Chir., V. 70, p. 762.
211. Hildebrand: Arch. f. klin. Chir., 81, 412.
212. Konig Paschen: Deutsche Ztschrft. f. Chir., V. 3. Schultze: Deutsche Ztschrft. f. Chir., 1877, V. 7. Reyber: Deutsche Ztschrft. f. Chir., V. 4.
213. Fessler: Deutsche Ztschrft. f. chir., V. 82.
214. Friedrich: Deutsche Ztschrft. f. Chir., V. 53. Friedrich u. Nosske: Ziegler's Beitr. z. pathol. Anat., 1899, V. 26. Muller: Deutsche Ztschrft. f. Chir., V. 25.
215. Jochmann and Batzner: Arch. f. klin. Chir., V. 95, p. 89.
216. Rost: Deutsche Ztschrft. f. Chir., V. 133.
217. Helferich: Chirurgenkongress, 1894; Arch. f. klin. Chir., V. 48.

218. Chlumsky: Zentralblatt f. Chir., 1900. Foderl: Ztschrft. f. Heilkunde, V. 16. Hofmann: Arch. f. klin. Chir., V. 80; Bruns Beitr., V. 59. Hubscher: Korrespondenzbl. f. Schweizer Ärzte, 1901. Lexer: Arch. f. klin. Chir., 95; Münchener med. Wchenschrft., 1913; Deutsche Ztschrft. f. Chir., 135; Zentralbl. f. Chir., 1917; Die freien Transplantationen Neue Deutsche Chir., V. 26 a, 1919. Roser: Zentralblatt f. chir., 1898. Payr: Münchener. med. Wochenschrft., 1910; Ztschrft. f. orthopad. Chir., V. 27; Arch. f. klin. Chir., V. 99; Deutsche Ztschrft. f. Chir., V. 129.
219. Murphy: J. A. M. A., 1905, p. 1573 and 1912, p. 985.
220. Homeyer and Magnus: Bruns Beiträge z. klin. Chir., V. 94. Segale: Bruns Beitr. z. klin. Chir., V. 87. Rehn: Chirurgenkongress, 1910, Arch. f. klin. Chir., V. 98. Sumitz: Arch. f. klin. chir., V. 99. Tappeiner: Arch. f. klin. Chir., V. 107.
221. Czerny: Arch. f. klin. chir., V. 13. Doutrelpout: Arch. f. klin. Chir., 9. Bier: Deutsche med. Wochenschrft., 1919, p. 620.
222. Schepelmann: Bruns Beitr. z. klin. chir., V. 108. Schmerz: Zentralbl. f. chir., 1916. Kocher: Chirurgenkongress, 1901.
223. Eisleb: Bruns Beitr. z. klin. Chir., V. 102.
224. Payr: Deutsche Zeitschrft. f. chir., V. 49.
225. Ledderhose: Deutsche Ztschrft. f. chir., V. 37. Franz, Arch. f. klin. Chir., V. 70.
226. Langemak: Arch. f. klin. Chir., V. 70.
227. Salkowsky: Compiled by Bier, Deutsche med. Wchenschrft., 1919, p. 620.
228. v. Langenbecks: Arch. f. Klin. Chir., V. 16.
229. Ollier: cited by Jogetho, Deutsche Ztschrft. f. Chir., V. 4.
230. Schmieden: Chirurgenkongress, 1913.
231. Kuttner: Arch. f. klin. Chir., V. 102; Zentralbl. f. Chir., 1911. Lexer: Arch. f. klin. chir., V. 90 and Med. Klink., 1908.
232. Borst: Pathologenkongress, 1912.
233. König: Zentralbl. f. chir., 1912.
234. Nobl: Der Varikose Symptomenkomplex lit., 2 ed., 1918.
235. Delbet: Sem. med., 1897.
236. Lowenstein: Mitt. a. d. Grenzgebieten, 1908, V. 18.
237. Braune: Festschrft. f. Ludwig, 1874.
238. Katzenstein: Zentralbl. f. Chir., 1911.
239. Schambacher: Deutsche Ztschrft. f. Chir., 1899, V. 53.
240. Ledderhose: Mitteil. a. d. Grenzgeb., 1906, V. 15.
241. Hasebrock: Deutsche Ztschrft. f. Chir., V. 136.
242. Trendelenburg: Bruns Beitr., V. 7, "Naturforscherversammlung," Leipzig, 1907.
243. Hoffmann: lit. Arch. f. Dermat., 1912, 113.
244. Kushimura: Virchows Archiv., 1905, 179.
245. Lesser: Virchows Arch., V. 101.
246. Zahn: Festschrft. f. Virchow, 2, p. 201. Eberth and Schimmelbusch: "Die Thrombose," Stuttgart, 1888. Ferge: Med. Naturh. Arch., V. 2. Beneke: Marchand-Krehl Handbuch. d. allg. Pathol., 22. Aschoff: Virch. Archiv., V. 130; Med. Klinik., 1909; Naturforscherversammlung, 1911.
247. Rost: Zieglers Beitr., 1911, V. 52.
248. Ribbert: Deutsche med. Wchenschrft., 1916, and Zentralbl. f. Pathologie, V. 27. Marchand: Zentralbl. f. Pathologie, V. 27, p. 193 and 457.
249. Rost: Zentralbl. f. Pathol., 1913.
250. Brucke: Virchows Arch., 1857, V. 12.

251. Zahn: Virch. Arch., 1875, V. 62.
252. Zurhelle: Ziegler's Beitrage, 1910, V. 47; Ztschrft. f. Gyn., 1908. Virchow: Ges. Abh. Frankfurt, 1856.
253. Huter: Allg. Chirurgie, 1873. Schwalbe: Ziegler's Beitr., V. 7.
254. Klebs-Welt: Zieglers Beitr., V. 4.
255. Enderlen: Deutsche Ztschrft. f. Chir., 1909, V. 99.
256. Stich: Bruns. Beitr., V. 53 and 62.
257. Silbermann: Virchows Archiv., V. 117. Kaufmann: Habilitationsschrift, Breslau, 1888. Lob: Bioch. Zentralbl., 1907, V. 6.
258. Ziemssen: Samml. klin. Vortr., 1887.
259. Landois: "Die Transfusion d. Blutes," Leipzig, 1875. Coca: Virchows Archiv., 1909, 196. Biedl-Kraus: Ztschrft. f. Immun. Forsch., 1910, V. 7.
260. Edelberg: Arch. f. exp. Pathol., 11. Angerer: "Klin. u. exper. Studien uber d. Resorpt. v. Blutextravasaten," Wurzburg, 1879.
261. Volcker: Chirurgenkongress, 1914.
262. v. Dering: cited by Hofmeister and Schreiber in Handbuch d. prakt. Chirurgie, V. 5, p. 7, 4th edition.
263. Wright: Journ. of physiol., 1891, 12.
264. Dietrich: Zentralbl. f. Pathol., 1912. Lob: Virchow's Arch., V. 153. Fromme: Naturforscherversamml., 1908. Heller: Bruns Beitr., 1909, V. 65. Jakowski: Zentralbl. f. Bakt., 25 and 28; Monatsschrift f. Gyn., V. 14. Bardeleben: Arch. f. Gyn., 1907, V. 83. Talke: Bruns Beitr., 1902, V. 36, p. 339.
265. Vaguez: These de Paris, 1890.
266. Trendelenburg: Prakt. Ergebnisse der Geburtshilfe u. Gynak., 1913.
267. Spalteholz: Arch. f. Anat., 1893, p. 1.
268. Quenu: Traite de Chirurgie de Duplay et Reclus, 1890, V. 2.
269. Schultz: Deutsche Ztschrft. f. Chir., V. 9. Greifenberger: Deutsche Ztschrft. f. Chir., V. 16. Riedel: lit. Deutsche Ztschrft. f. Chir., 1876, V. 6.
270. O. Weber: in Pitha-Billroth's Handbuch der Allg. spez. Chir., 1865.
271. Katzenstein: Deutsche Ztschrft. f. Chir., 1905, V. 77, p. 189.
272. Bier: Deutsche Ztschrft. f. Chir., V. 79.
273. v. Recklinghausen: Deutsche Chir., V. 2 and 3. Nothnagel: Ztschrft. f. klin. Med., V. 15 and 17, suppl.
274. Katzenstein: Deutsche Ztschrft. f. Chir., V. 80.
275. Krehl: "Pathol. Physiologie," F. C. W. Vogel, Leipzig, trans. Hewlett.
276. De Ahna: Pflugers Arch. f. d. ges. Physiol., V. 12. Zuntz: Pflugers Arch. f. d. ges. Physiol., V. 17.
277. Jordan: Bruns Beitr., V. 14, p. 279. Goldmann: Bruns Beitr., 1905, V. 47, p. 162. Niebergall: Deutsche Ztschrft. f. Chir., V. 33, p. 540 and V. 37, p. 268.
278. Wieting: Deutsche med. Wochenschrft., 1908, V. 28. Deutsche Ztschrft. f. Chir., V. 110.
279. Exner: Wiener klin. Wchenschrft., 1903.
280. Verth: Deutsche Ztschrft. f. Chir., V. 151.
281. Israel: Deutsche Ztschrft. f. Chir., V. 149. Franz: Arch. f. klin. Chir., V. 75. Muck: Munchener Med. Wchenschrft., 1916. Vignolo: Policlinico, 1902. Bramann: Arch. f. klin. Chir., V. 33, lit. Wahl: Deutsche Ztschrft. f. Chir., V. 21.
282. Th. Weber: Cited by Sahli, Lehrbuch d. klin. Untersuchungsmethoden, 6 edition.
283. Brugsch-Schittenhelm: Lehrbuch d. klin. Untersuchungsmethoden, 1908, V. 110.
284. Wertheim: Annales de Chemie and de Phys., 1847. Botticher: Deutsche Ztschrft. f. Chir., V. 49.

285. Heinecke: Deutsche Chir., V. 18, p. 11.
286. Beyme: Deutsche Ztschrft. f. Chir., V. 140.
287. Eschweiler: Deutsche Ztschrft. f. Chir., V. 23.
288. Halban: Arch., f. klin. Chir., V. 55. Wiener klin. Wchshrft., 1898. Manfredi: Virchow's Arch. V. 155. Viola, Ztschrft. f. Hyg., V. 30. Notzel: Arch. f. klin. Chir., V. 81. Bruns Beitr., V. 51 and 65.
289. Zehnder: Virchows Arch., V. 120. Bayer: Arch. f. klin. Chir., V. 49. Ritter: Deutsche Ztschrft. f. Chir., V. 79. De Vecchi: Mitt. a. d. Grenzgeb., V. 23. De Groot: Deutsche Ztschrft. f. Chir., V. 119 and 122.
290. Gross: Deutsche Ztschrft. f. Chir., V. 127 and 138. Arch. f. klin. Chir., V. 76 and 79.
291. Cohnheim: Virchows Archiv., V. 47.
292. Gobel: Ergeb. d. Chir., 2. Rost: "Fiber Flariasis," Klin. Therapeut-Wchnschrft., 25.
293. Winiwarter: Deutsche Chir., V. 23. Draudt: Ergeb. d. Chir., V. 4. Helffuch: Inaug. Dissert. Heidelberg, 1919 for lit.
294. Carle and Jambon: Gaz. des. Hospiteaux, 1904.
295. Bockhardt: Monatsschrft f. prakt. Dermat., 1883.
295. Bramann: Munchener med. Wochenschrft., 1902. Favarger: Wiener klin. Wchnshrft., 1901. Kuhn: Wiener klin. Wchenschrft., 1905. Schmidt: Bruns Beitr., V. 44.
296. Rost: Munchener med. Wchenschrft., 1918.
297. Nonne: Virchows Archiv., 125. Reinsbach: Bruns Beitr., 1898, V. 20.
298. Lanz: Zentralbl. f. Chir., 1911, 1 pt. Kondolean: Munchener med. Wchenschrft., 1912 and 1915.
299. Carnochan: Cited by Winiwarten, l. c.
300. v. Eiselsberg: Wiener klin. Wochenschrft., 1906.
301. Freytag: Diss. Bonn., 1891. Sternberg: Nothnagels spez. Path. and Therapie, V. 7, 2.
302. Ebstine: Arch. f. klin. Med., V. 89, p. 67 for complete lit. Mitteil. a. d. Grenzgebieten, V. 22, p. 311.
303. v. Hoffmann: Arch. f. klin. Med., 1919, V. 130, p. 201.
304. Braun: Med. Klinik., 1918, pt. 1.
305. Bamberger: Ztschrft. f. klin. Med., 1891, V. 18.



## INDEX OF AUTHORS

---

- Abderhalden, Emil, 41, 57, 67, 112, 127,  
     193  
 Abderhalden, E. and London, 112  
 Adamkiewicz, 403, 417  
 Adamski, Johann, 114  
 Adler, 314, 317, 357, 360  
 Adrain, 256, 257  
 Aeby, 428  
 Aksne, 302  
 Albarran, 281, 285, 293, 309  
 Albarran and Guyon, 301  
 Albeck, Ileus, 225  
 Albert, 18  
 Albert and Schnitzler, 408  
 Alberts, G., 71  
 Albrecht, P. A., 53, 151  
 Albu, 208, 225, 265  
 Albu and Kretschmer, 209  
 Albu and Lexer, 269  
 Aldrich, 233  
 Alexander and Reko, 6  
 Alexandre, 12  
 Allard, 284, 285  
 Allen, 322  
 Alvarez, 44, 45, 61  
 Alzheimer, 416  
 Anders, 423  
 Andreson, 340  
 Andrews, 231  
 Angerer, 474  
 Anghel, 257  
 Anschutz, W., 205, 222  
 Antonini, L., 76  
 Aoyama, T., 133  
 Aquapendente, Fabricius ab, 177  
 Archibald, Edward, 102, 103  
 Aristotle, 176  
 Arnd, 241  
 Arnold, 119, 391  
 Asakura 292  
 Aschoff and Bacmeister, 113, 132, 133  
 Aschoff, L., 124, 134, 256, 260, 263, 472  
 Aschoff, Ludwig, 37, 40  
 Ascoli, 287  
 Ash, 312  
 Asher, 148, 153  
 Asher and Flack, 340  
 Asher and Spiro, 171  
 Askanazy, 249  
 Auché, 8  
 Auerbach, 12  
 Aufrecht, 134, 301  
 Axhausen, 264, 266, 415, 446, 449  
 Axhausen and Pels, 447  
 Babera, 125  
 Babes, 421  
 Babkin, B. P., 41, 49, 81, 123, 190  
 Baetzner, 279  
 Baggerd, 298  
 Bahr, 443  
 Bail, 242, 246  
 Bainbridge and Dale, 126  
 Bajardi, 435  
 Bakes, 179, 292  
 Balser, 102  
 Baltzner, 279  
 Bamberger, 482  
 Banti, 156  
 Baracz, 192, 215  
 Barbarossa, 356  
 Barbera, 124, 125  
 Barcroft, J., 378  
 Bardach, 153  
 Bardeleben, 330, 475  
 Bardenheuer, 440, 450, 458  
 Barie, 366 (ref. 402)  
 Barker, 267  
 Barnabo, 463  
 Baron, 120  
 Barsony, Theodor, 56  
 Bartel, 320  
 Bartels, 327  
 Barth, 101, 295, 296, 365 (ref. 402), 448  
 Baruch, 348  
 Basch, 351

- Bauer, 298, 324, 326, 355, 362, 416, 442, 448  
 Bauer, Julius, 53, 77, 78, 130, 248, 267  
 Bauereisen, 305  
 Bauhin, 176  
 Baum, 239, 293  
 Baumann, 338  
 Baumgarten, 309, 310, 311  
 Bayer, R., 149, 152, 153, 155, 157, 222, 431, 480  
 Bayliss, W. M. and Starling, E. H., 43, 44, 57, 194, 197, 198  
 Bayon, 341  
 Beattie, 179  
 Beaumont, Wm., 81  
 Beaussenat, 257  
 Beck, 25, 320, 412  
 Becker, 294, 318, 394, 433, 460, 461  
 Begrer, 410  
 Beirn, O., 200, 217  
 Bell and Hirschberg, 267  
 Beloussow, 130  
 Bencke, R., 76, 165, 190, 391, 392, 394, 395, 445, 472  
 Benker, 180  
 Berard and Petel, 277  
 Beresnegowsky, 267, 268  
 Berg, 138  
 Berg, A. A. H. and Snapper, I., 129  
 Berger, 157  
 Bergmann and Bastgen, 407  
 Bergmann, G., 76, 78, 176, 277, 341, 357, 403, 411, 420  
 Bergmann and Guleke, 114  
 Bergmann and Lenz, 200  
 Bernard, A., 24  
 Bernard, Claude, 1, 5, 6, 68, 69, 111, 117, 119, 127, 282, 349, 433  
 Bernard and Salomon, 309  
 Berndt, 320  
 Bert, Paul, 372  
 Bertelle, G. and Falta, W. and Schweeger, O., 149  
 Bertelsmann and Man, 307  
 Berth, 11  
 Berthier, 454  
 Berthold, 329  
 Bertog, J., 138  
 Besancon and Griffon, 74  
 Best, 70  
 Best, F. and Cohenheim, O., 36  
 Bethe, 456, 457  
 Bethe and Parnas, 430  
 Beyme, 479  
 Bial, 184  
 Biberfeld, 292  
 Bibergeil, 162  
 Bickel, A., 42, 58, 63  
 Bidder, 435  
 Biedl, 7, 98, 99, 289, 323, 324, 326, 327, 339, 340, 341, 342, 351, 359, 362, 364  
 Biedl and Kraus, 304, 307, 474  
 Bier, 52, 234, 419, 435, 449, 455, 460, 468, 477, 479  
 Biernacki, E., 5, 42  
 Biers, 461  
 Billard and Cavillie, 135  
 Billroth, 9  
 Bing, 428  
 Binswanger, 416, 417  
 Bircher, H., 14, 342, 344, 345, 352, 354, 361, 363, 415  
 Birkenbach, 287  
 Bittorf, 254, 372  
 Bittorf and Forschbach, 386  
 Blad, 139  
 Blaue, 199  
 Blaue and Reich, 344  
 Blaue, Muller and Schlager, 354  
 Blayney, 265, 266  
 Blenkle, 453  
 Blessing, 458  
 Blevgad, 415  
 Bloch, 198, 436  
 Blum, 339  
 Blumenfeldt, 157  
 Boas, I., 60, 209  
 Bockhardt, 481  
 Bode, 365 (ref. 402)  
 Bocckel, 460  
 Boehm, 198, 209  
 Boeke, 430, 457  
 Boenninghaus, 415  
 Boetzel, 303  
 Bogen, H., 42  
 Bogoljuboff, 330  
 Bohl, 411  
 Bohm, P., 125, 366 (ref. 402)  
 Bohn, 140  
 Bohr, 372, 380  
 Boldgreff, 357  
 Bollinger, 414

- Bolton, 78  
 Bonchardal and Sandras, 97  
 Bonin, 74  
 Bonneken, 241  
 Bonnet, 443  
 Borbjarg and Fischer, 184  
 Borchard, 414, 455  
 Borchardt and Wjasmenski, 457  
 Borchers and Klatsch, 194  
 Bordenheuer, 253  
 Bordet, 244, 246  
 Borggreve and Hessel, 217  
 Borgzecky, 300  
 Borst, 170, 469  
 Borst and Enderlen, 293  
 Borszeky and Genersich, 225  
 Borzeky, 56, 63, 225  
 Bose and Heyrovsky, 196  
 Botticher, 479  
 Bouchard, 225, 287  
 Bouisson, 238  
 Bouma, 391  
 Bourdenko, 117  
 Bouveret, 384, 385  
 Boyer, 201  
 Boysen, I., 133  
 Braatz, 295  
 Bradford, 286  
 Bramann, 478, 479, 481  
 Bramann and Rammstedt, 324  
 Brand, 125, 320  
 Brandes, 438  
 Brandl, 320  
 Brauer, 366, 374, 378, 379, 380, 382, 383  
 Brauer and Roth, 378  
 Braun and Boruttau, 225, 226, 227, 248, 249, 250  
 Braun and Heinrich, 63, 71, 416, 422, 464, 482  
 Braun and Honckgeest, 44  
 Braun, Tuffier and Payer, A., 51  
 Braun, W. and Seidel, H., 51, 52  
 Braune, 470  
 Brauning, H., 38  
 Braunschweig, 152  
 Braus, 429, 457  
 Breitner, 344  
 Bremer, F., 96  
 Brenner, A., 79, 264, 266  
 Breslauer, 403, 407, 408, 409, 410, 413, 460  
 Breton, M., 97  
 Bretonneau, 365  
 Breus, 75  
 Bright, 414  
 Broca, 449  
 Broca and Tridon, 462  
 Brodmann, 421  
 Brogsitter, 151  
 Brohmman, 176, 177  
 Bronadel, 14  
 Brosch, 29  
 Brown, 229  
 Brown and Sequard, 289, 318, 417, 438  
 Bruce, 460  
 Brucke, 163, 165, 473  
 Brugsch, 267  
 Brugsch and Klemperer, 313  
 Brugsch and Schittenhelm, 479  
 Brun, H., 80  
 Brun, Max, 46  
 Brunacci, 2  
 Brunn, 256, 259, 306, 321, 411  
 Brunner, 241, 454  
 Bruns, 60, 358, 378, 382, 384  
 Bruns and Saurbruch, 384  
 Buch, 172, 174  
 Buchanan, 253  
 Buchbinder, 242  
 Buchner, 246, 462  
 Buchwald and Litten, 293  
 Budinger, 448  
 Bumm, 318, 438  
 Bungart, 404, 406  
 Bunge, 104, 122, 231, 298  
 Burchardt, 242  
 Burci, 161  
 Burger and Fischer, 130  
 Burkhardt, 162, 183, 374, 378  
 Burn, 179, 438  
 Burrow, 407  
 Buru, 438  
 Busch, 217, 315, 392, 463  
 Busch and Biebergeil, 162  
 Buschan, 346  
 Busse, W., 72, 74, 236, 392, 393  
 Bussman, 442  
 Buttermann, 11  
 Buxton, A. St. C., 6  
 Cahn, 17  
 Cammerer, 75  
 Camus, L. and Gley, E., 97

- Cannon, W. B., 37, 39, 40, 44, 47, 50, 194  
 Cannon, W. B. and Blake, J. B., 56  
 Cannon and Moser, 21  
 Cannon and Murphy, 52  
 Canon, 244  
 Capelle and Bayer, 350, 351, 352, 353  
 Carle and Jambon, 481  
 Carlson, 47, 48, 66  
 Carlson and Luckhardt, 25, 40  
 Carlsson, 180  
 Carnochan, 482  
 Carnot, 104  
 Carriere, G., 4  
 Casagli, F., 58  
 Cassirer, 414, 459  
 Cathelin, 309  
 Cecca, 464  
 Cervells, 388  
 Chalatoff, 133  
 Championiere, Lucas, 440  
 Chantemesse and Widai, 74  
 Chaput, 233  
 Charcot, 438, 459  
 Charrin, 74, 257, 418  
 Chassaignac, 460  
 Chauffard, 132  
 Chiari, 103, 118, 398  
 Chittenden and Richards, 3  
 Chlumsky, V., 54, 58, 60, 467  
 Christiani and Kummer, 342  
 Chrobak, 251, 253  
 Chvostek, 346, 359, 362  
 Clairmont and Haberer, 131, 139, 167, 169, 245  
 Clairmont, P., 3, 4, 71, 80, 386, 395, 421  
 Clairmont and Ranzi, 229, 249  
 Claisse, P. and Dupre, E., 8, 13  
 Clark, 253  
 Clerk, A. and Loeper, 97  
 Cloett, 379  
 Cobbet and Valte, 230  
 Coca, 474  
 Coenen, 297, 298, 444, 463  
 Cohn, M., 29, 66, 81, 293, 305, 355  
 Cohnheim, 190, 192, 201, 285, 288, 365 (ref. 402, 481), 395  
 Cohnheim, Julius, Fredrich, 59, 76  
 Cohnheim and Litten, 118  
 Cohnheim and Marchand, 41, 137  
 Cohnheim, Otto, 37, 38, 40, 41, 96, 98  
 Cohnheim, O. and Klee, P., 57, 96, 126  
 Cohnheim and Roy, 283  
 Colasanti, 124  
 Coller and v. Schjerning, 411  
 Condray, 312  
 Connor, O., 350  
 Conrad, 459  
 Conradi, H., 134, 305  
 Contejean, 70  
 Copemann and Winston, 126  
 Cordier, 381  
 Cordua, 163  
 Corneliani, 479  
 Corner, 255  
 Cornil and Carnot, 179  
 Cornil and Condray, 448  
 Corning, 14  
 Cosenthino, 120  
 Councilmann, 463  
 Courmont and Gabonlay, 461  
 Courtade, D. and Guyon, J. F., 43, 126  
 Courvoisier, 128  
 Couvelaire, 16  
 Cozzolino, 303  
 Crede, 152  
 Crile, 229  
 Curschmann, 362, 364, 385  
 Curtis, 149  
 Cushing, 403, 407, 413  
 Cushing and Livinggood, 241  
 Cushny, A. R., 279, 280  
 Cuvier, 177  
 Czermak, 17  
 Czerny, 151, 155, 394, 468  
 Dagaew, W. F., 57, 64, 66, 68  
 Dal Fabbro, 12  
 Dalla Vedova, R., 76  
 Damascelli, 436  
 Danielsen, 167, 168, 186, 363  
 Danilewsky, 68  
 Danilewsky and Selensky, 150  
 Dastre, 58, 126, 127  
 Dauriac, 199  
 David, 196  
 Davis, N. C., Hall, C. C. and Whipple, G. H., 115  
 Dax, 436, 455  
 De Ahna, 477  
 Deaver, J. B. and Sweet, J. E., 102  
 Debaisieux, 314  
 Decastello, H., 157



- Decker, J., 74  
 De Dominici, 98  
 de Filippi, F., 66  
 De Groot, 480  
 Delbert, 478  
 Delbet, 356  
 Delezenne, C., 97, 127  
 Delkeskamp, 455  
 Del Vecchio, 365, 480  
 Demarquai, 318  
 Demme, 460  
 De Meyer, 98  
 Deneke, 355  
 Denk, 264, 265, 266, 267  
 De Quervain, 323  
 Deroche, 438  
 Dette Santi, 312  
 Deucher, 409  
 De Vecchi, 481  
 De Voogt, 136  
 De Witt, 20  
 Dieterle, Hirschfeld and Klinger, 342, 344  
 Dietl, 300  
 Dietlen, 199  
 Dietler, 23  
 Dietrich, 475  
 Dieulafoy, 258  
 Diliberti and Herbin, 265  
 Disse, 71, 282, 283  
 Dittel, 320  
 Dittrich, P., 8  
 Doberauer, 105  
 Doenitz, 415  
 Doepfner, 412  
 Dogiel, 126, 380  
 Doll, 298  
 Donati, Mario, 76  
 Donders, 374  
 Doutrelpout, 468  
 Doyen, 60  
 Doyon, 115, 126  
 Doyon and Dufort, 125  
 Draudt, 481  
 Dreike, 190  
 Dreyer, 223, 464, 465  
 Dreyfuss, 413  
 Droge, 148, 155  
 Drumond, 122, 179  
 Dubar and Remy, 167  
 Du Bois and Reymond, 372, 431  
 Duccesi, Virgilio, 39, 44  
 Dudgeon and Roos, 179  
 Dunin, 301  
 Duplay, 439  
 Durck, 396  
 During, 474  
 Eastman, 419  
 Eastmann, 210  
 Eberle, 97  
 Ebert, 379, 380  
 Eberth and Schimmelbusch, 472  
 Ebstein, 482  
 Ebstein and Nicolaier, 314  
 Ebstein, Wilhelm, 76, 208, 313, 349  
 Eckhard, 282, 285  
 Edelberg, 474  
 Edebohl, 292  
 Eden, 435  
 Edinger, 3, 68, 456  
 Edkins, J. S., 41  
 Egau, E., 39  
 Ehret and Stolz, 134  
 Ehrhard, 140  
 Ehrhardt, 116, 117  
 Ehrlich, 148, 149, 150  
 Ehrmann, 14, 17, 101  
 Eichel, 230  
 Einhorn, 203  
 Einthoven, 375  
 Eiselsberg, 326, 342, 360, 363, 482  
 Eiselsberg, Freiherr, 72, 177  
 Eisenmenger, 119  
 Eisleb, 468  
 Eliasberg, 155  
 Ellenberger, 38, 42  
 Elliot, 152, 314  
 Elliot, T. R. and Smith, E. B., 43, 194, 198  
 Elmendorf, 289  
 Elsberg, 365 (ref. 402)  
 Elze, 37  
 Emelianoff, 152  
 Enderlen, 22, 179, 190, 296, 301, 302, 321,  
     328, 342, 421, 422, 461, 469, 474  
 Enderlen and Hess, 196  
 Enderlen, Hotz, and Magnus Alsleben,  
     118, 121, 123, 192, 213, 214, 221, 226,  
     249, 250  
 Enderlen and Justi, 140  
 Enderlen and Zumstein, 138  
 Engelhardt, G. and Neck, K., 72  
 Engelhorn, 173

- Engelmann, 302  
 Englisch, 463  
 Engstrom, 241  
 Eppinger, 128, 129, 340, 341, 385  
 Eppinger and Hess, 78, 349, 388  
 Eppinger and Hofbauer, 378, 387  
 Eppinger and Ranzi, E., 156  
 Erdheim, 359, 362  
 Erhard, 119, 140  
 Erkes, 242  
 Erlacher, 435, 456  
 Erlanger, 456  
 Erlanger and Hewlett, 266  
 Ernst, 391, 394  
 Esau, 190, 255  
 Escherich, 99, 362  
 Eschweiler, 479  
 Esmarch, 267  
 Eulenberg, 346, 463  
 Evans and Brenizer, 267  
 Ewald, 123, 264, 342, 343  
 Exalto, 63  
 Exner, 491  
 Exner, Alfred, 43, 49, 478  
 Exner, A. and Heyrowsky, H., 132  
 Exner, A. and Jaeger, 44, 172  
 Exner, A. and Schwarzmnn, 49  
 Eykmann, 16, 18  
  
 Falloise, 225, 226  
 Falta, 341, 359  
 Falta and Kahn, 362, 363, 364  
 Falta and Rüdinger, 363, 364  
 Faltin, R., 151  
 Faulhaber, 37  
 Faulhaber, M. and Redwitz, E. F., 65  
 Favarger, 481  
 Felizet, 411, 412  
 Feltz and Ritter, 287  
 Fenwick, 71  
 Ferge, 472, 473  
 Ferrarin, 292  
 Ferrier and Adam, 230  
 Fessler, 466  
 Fibich, R., 71, 79  
 Fibiger, 393  
 Fick, A., 373, 428, 429, 430, 443  
 Fick and Gabler, 429  
 Fick, R. and Strasser, 429, 444, 467, 468  
     469  
 Filehne, 349  
 Filehne and Ruschhaupt, 285  
 Finger, 316  
 Finkelnburg, 408  
 Finkelstein, 362  
 Finsterer, 140, 181  
 Fiori, 295  
 Fischer, 444  
 Fischer, Georg, 364, (ref. 402, 366  
 Fischer, O., 431, 438  
 Fischer and Benzon, 299  
 Fischl, 264, 298  
 Fischler, F., 105, 110, 111, 112, 113, 118,  
     119, 121, 124, 128, 211, 357  
 Fisher, 411, 450  
 Flechtenmacher, 66  
 Fleckseder, R., 3, 4, 5, 6, 99, 100  
 Fleig, 96  
 Fleiner, W., 23, 37, 38, 184, 209, 361  
 Fleischl, 128  
 Flint, 267  
 Florain, L., 3  
 Florchen, 136, 292  
 Florken, 136  
 Flourens, 457  
 Flugge, 463  
 Foderl, 467  
 Forderreuther, 175  
 Forssel, Gosta, 37  
 Forster, I., 134, 422, 444, 458  
 Forster, O. and Kuttner, H., 46, 49  
 Foulerton and Hillier, 308  
 Fraenkel, E., 353, 462  
 Francke, 306  
 Frank, 308, 328, 350, 430  
 Franke, 123, 173, 239, 254, 261, 303, 304,  
     397, 436  
 Franke and Rabe, 119  
 Frankel, 28, 139  
 Frankel, J., 139  
 Frankel and Krause, 134  
 Frankfurter, 359  
 Frankl and Hochwart, L. and Fohlich, A.,  
     43, 201, 314, 316, 326, 359, 361  
 Fransen, 176  
 Franz, 412, 478  
 Fratlin, 453  
 Fredericq, 376  
 Freiberg, 155  
 Frerichs, 130, 286, 391  
 Freudenberg, 319  
 Freund, W. A., 165, 387, 388

- Frey, 193, 433, 434, 439  
 Frey and Harley, 130  
 Frey and Lury, 157  
 Freyer, 322  
 Freytag, 482  
 Friedemann, U., 97  
 Friedjung, 354  
 Friedlander, 248, 414  
 Friedmann, 97, 413  
 Friedrich, 177, 241, 253, 256, 358, 372,  
     380, 382, 383, 385, 414, 420, 421, 466  
 Friedrich and Nosske, 466  
 Frisch, 322  
 Fritsch, 49  
 Fritsch and Hitzig, 417  
 Fritsche, 392  
 Frohlich, 327, 350  
 Frohlich and Meyer, 175, 314, 316  
 Fromme, 303, 475  
 Fuchs, 459  
 Fuld, 429  
 Funke, 255  
 Furbringer, 323  
 Furnohr, 437  
 Fursterer, H., 79  
 Furth, 346, 348  
 Futterer, 77  
  
 Gaetani, 282  
 Galen, 176  
 Galeni, 408  
 Galippe, 12  
 Gama and Alquie and Felizet, 411  
 Gant, 206, 207  
 Garnier, 226  
 Garre, C., 100, 351  
 Garre and Eckhardt, 300  
 Garre and Quincke, 372, 383  
 Gaultier, 2, 10  
 Gawrilow, 292  
 Gayett and Bonnet, 441  
 Gebele, 352, 397  
 Gegenbauer, 171  
 Geigel, 403, 407  
 Gelle, 99  
 Gelpke, 293  
 Genersich, 199, 225, 227  
 Gerhard, 381  
 Gerhard, 378, 379, 380, 385, 387  
 Ghedini, 264  
 Ghillini, 429  
  
 Ghiron, 283  
 Gies, 446, 448, 465  
 Giesoro and Hahn, 14  
 Girard, 30  
 Girgloff, 292  
 Glaessner, 134  
 Glaserfeld, 353  
 Glassmer, 96  
 Glassner, 134, 196  
 Glassner, K. and Singer, G., 127  
 Glenard, Frantz, 53, 184  
 Gley, 96, 348, 359  
 Glimm, 169, 246  
 Glinski, 191  
 Glisson, 176  
 Gluck, 110, 435  
 Gobel, C., 135, 207, 435, 481  
 Gocke, C., 64, 65  
 Goebel, 312, 329, 397  
 Goetzl and Israel, 283  
 Goldmann, 478  
 Goldschmidt, 321  
 Golowiewff, 122  
 Goltz, 20, 24, 201, 417  
 Goltz, F., 43, 201  
 Goppert, 304  
 Goringstein, 366 (ref. 402)  
 Gosselin, 460  
 Gosset, A., 61  
 Gossmann, T. R., 75  
 Goto, 453  
 Gottlieb, 338, 339, 350  
 Gottlieb and Sicher, 23  
 Gottstein, 23, 24, 27, 279, 281  
 Graser, F., 54, 285  
 Grashey, 406  
 Grassi and Munason, 344  
 Gratz, 362, 363, 364, 384  
 Grawitz, 243, 442, 463  
 Grawitz and De Barry, 463  
 Grawitz, F. and Steffen, W., 3  
 Greifenberger, 476  
 Greyerz, 222  
 Grodel, 199  
 Grodel, F. M. and Seyberth, L., 36, 206  
 Groedel, F. M., 37  
 Grohe, B., 66  
 Grondahl, 392, 393  
 Gross, 101, 279, 281, 480, 481  
 Gross, O., 154  
 Gross, Walter, 41

- Grossmann, 438  
 Gruber, 220, 454, 459  
 Grunberg, 155  
 Grunert, 323  
 Grunewald, 428, 437, 441, 444  
 Grutzner, 5, 38, 42, 97, 194, 430  
 Grutzner, P., 38  
 Guelke, 359  
 Guerin, 8  
 Guiscz, 28  
 Guiteras, 293  
 Guleke, 183  
 Guleke, N., 101, 104, 114, 363  
 Gundelfinger, E., 76  
 Gundermann, W., 78, 177, 287  
 Gussenbauer, 64, 463  
 Guyon, 309, 322
- Haab, 435  
 Haberer, H., 52, 61, 63, 64, 74, 78, 116, 286, 295, 297, 301, 351  
 Haberfeld, 360, 361  
 Haberland, 435  
 Hacker, 28, 446  
 Hadda, 181  
 Hagenbach, 341  
 Hagenbach and Burckhardt, 428  
 Hagler, 247  
 Haguenot, 250  
 Hahn, 450  
 Haim, 240, 256  
 Hainski, 119  
 Halban, 14, 480  
 Haldane and Douglas, 372  
 Hallendahl, 10  
 Haller, 406  
 Hamburger, 192, 224  
 Hammar, 351  
 Hammarsten, O., 4, 124, 127, 135  
 Hanau, 8, 10, 329, 341  
 Handel, 134  
 Handley, W. S., 123  
 Hanseemann, 134, 388  
 Hansen, 308  
 Hari, 422  
 Harrison, 291, 456  
 Hart, 76, 342, 351, 352, 353, 356  
 Hartel, F., 65  
 Hartl, 383  
 Hartmann, 463  
 Hartmann and di Gasparo, 416, 418
- Hartmann, H. and Soupault, M., 56  
 Hartmann and Mignot, 258  
 Hartseemann, 256  
 Hasebrock, 471  
 Hasse, 378  
 Hasselbach, 375, 376  
 Haukin, 246  
 Hauptmann, 403, 404, 407, 408, 411  
 Haurrel, 12  
 Hauser, G., 72, 413  
 Hayem, 54  
 Head, 46, 175  
 Hedon, 98  
 Heger, 178  
 Heidelberg, 450  
 Heidenhain, 1, 6, 95, 96, 221, 225, 438, 439, 444  
 Heilberg, K. A., 95, 99  
 Heilbronner, 418  
 Heile, 193, 199, 240, 255, 256, 257  
 Heine, 469  
 Heineke, H., 1, 8, 9, 10, 12, 96, 100, 215, 248, 422, 456, 479  
 Heinlein, 28  
 Heinsheimer, F., 57  
 Heinz, 161  
 Hekma, E., 97  
 Helferich, 435, 466, 467  
 Helfuch, 481  
 Hellendahl, 9  
 Heller, 23, 119, 299, 391, 475  
 Heller and Weiss, 24  
 Helly, 151  
 Helmholtz, 434  
 Hemmeter, J. C., 7  
 Hendel, 134  
 Henderson, L. J., 291  
 Henderson, Y. and Haggard, H. W. and Coburn, R. C., 229, 291, 377  
 Henke, 432  
 Henle, 250  
 Henle and Heile, 397  
 Henle and Krauss, O., 199  
 Henri and Portier, 125  
 Hensing, 176  
 Henzelmann, 373  
 Herb, E., 9  
 Hering, 356  
 Hering and Brener, 375  
 Herman and Escher, 419  
 Hermann, 192, 295, 296, 374, 411



- Hernheimer and Hall, 292  
 Herre, 56  
 Hertle, 231  
 Hertz, Arthur F., 206, 207, 208, 211  
 Hertz, Axtel, 61  
 Herz, 444  
 Herzfeld and Klinger, 165  
 Hess, 101, 110, 176  
 Hesse, 55, 180, 344  
 Hesselbach, 376  
 Heukelom and Siegerbeek, 130  
 Heusner, 167, 177, 178  
 Heuter, 429, 432  
 Heyde, 227, 240, 253, 256, 295  
 Heyde and Vogt, 287  
 Heyrowsky, 23  
 Hildebrand, 104, 298, 349, 350, 443, 448,  
     451, 452, 455, 466  
 Hildebrand and Haga, 301  
 Hildebrand, Scholz and Wieting, 449  
 Hildebrandt, 435  
 Hill, 403, 409  
 Hill and Ziegler, 405  
 Hilty, 435  
 Hippocrates, 9  
 Hirsch, 224, 304, 312, 342, 365, 382  
 Hirschel, 20  
 Hirschel, G., 140, 162, 167  
 Hiss, 456  
 Hlava, 104  
 Hochenegg, 79, 181, 220, 326, 327  
 Hochstetter, 73  
 Hoehne, 170  
 Hoenck, 260  
 Hoessly, 409, 410  
 Hofbauer, L., 3, 132, 372, 373, 378, 381,  
     386  
 Hoffa, 448  
 Hoffmann, 72, 175, 380, 388, 459, 472, 482  
 Hoffmann, A., 238  
 Hoffmann, F. A., 388  
 Hofmann, F., 467  
 Hofmeister, 341, 474  
 Hofmeister, Franz, 37  
 Hofmohl, 218  
 Hofstadter, 350  
 Hohlweg, H., 111, 135, 137  
 Holder, 414  
 Holmberg, 99, 100  
 Holmgren, 351  
 Holscher, 395, 396  
 Holterhof, 361  
 Holzknecht, 36, 194, 197, 209  
 Holzknecht, G. and Luger, A., 38, 51  
 Holzknecht and Jonas, 37, 40  
 Holzknecht and Olbert, 25  
 Holzmann, 404  
 Homburger, 315  
 Homeyer, 100  
 Homeyer and Magnus, 467  
 Hopfner, E., 120, 122  
 Hoppe-Seyler, 395  
 Hormann, 181, 183  
 Hormuth, 463  
 Hornborg, A. F., 42, 81  
 Hornemann, 305  
 Horsley, 326, 338  
 Horvart, 437  
 Hotz, G., 62, 70, 213, 221, 249  
 Houel, 320  
 Howell, 320  
 Hubscher, 467  
 Hunt, Reid, 339  
 Hunter, 69  
 Hurley, 128  
 Huter, 473  
 Hyrtl, 364  
 Ianson, 116, 117  
 Ibrahim, 50  
 Ijzeren, W., 76, 79  
 Ikonnikof, 241  
 Ingianni, 321  
 Isaac, S., 111, 157  
 Isaef, 244  
 Iselin, 251, 360  
 Isenschmid, 342  
 Isler, 255  
 Isobe, 292, 294  
 Isobeleff, 101  
 Israel, 165, 292, 293, 304, 309, 478, 479  
 Ito, H. and Asahara, S., 66, 419, 420  
 Ito and Omi, 121  
 Jackson, 417  
 Jacobs, 27  
 Jacobs, M. H., 377  
 Jacobson, 329  
 Jaffe, 164, 464  
 Jager, 378  
 Jagetho, 469  
 Jakowski, 475

- Jamin, 441  
 Janeway and Ephraim, 229  
 Janis and Nakarais, 312  
 Jansen, 444  
 Januschke, H., 76, 77  
 Jappeli, G., 3  
 Jawein, 3, 6, 150  
 Jeannel, 269  
 Jehle, 298  
 Jehn, 287, 395  
 Jehn and Naegeli, 395  
 Jenckel, 283  
 Jensen, 242, 244  
 Joachimsthal, 423, 429  
 Jochmann, 385  
 Jochmann and Batzner, 466  
 Jonas and Rudinger, 362  
 Jonas, S. and Holzknecht, G., 37  
 Jordan, 264, 307, 478  
 Josselin de Jong, 118, 121  
 Josselin de Jong and Sax, R., 118  
 Jousset, 308  
 Jungling, 453  
 Jungmann, 282  
 Jungmann and Meyer, 282  
 Justi, 192  
  
 Kader, 213  
 Kafemann, 260  
 Kahler, 421  
 Kahn, 19, 20, 314  
 Kaiser, F. F., 66  
 Kaoru, Omi, 193  
 Kaplan, S., 64, 65  
 Kappis, 29, 172, 283, 311  
 Kapsammer, 284, 285, 301, 436  
 Karlinski, 242  
 Karplus and Kreidl, 315  
 Kast and Meltzer, 173, 175  
 Kastle, 37, 38, 39  
 Kastle, C., Rieder, H. and Rosenthal, I.,  
     37, 38  
 Kathe, H., 62  
 Katschkowsky, P., 49  
 Katz and Winkler, 199  
 Katzenstein, M., 57, 58, 62, 70, 80, 292,  
     470, 477  
 Kauffman and Ruppner, 364  
 Kaufmann, 23, 24, 68, 73, 204, 474  
 Kaufmann, Eduard, 73  
 Kausch and Kaplan, 57  
  
 Kausch, W., 56, 60, 79, 138  
 Kavasoye, 302  
 Kawamura, K., 70, 76  
 Kazmelon, Helene, 21, 81  
 Kehr, 110, 116, 117  
 Kehr, J. K., 70  
 Keller, Katharina, 374  
 Kellie, 419  
 Kelling, Georg, 22, 51, 55, 56, 58, 59, 61,  
     181, 183, 397  
 Kemp, S., 80  
 Kempf, 231  
 Kendall, E. C., 339  
 Kepinow, 350  
 Kermauner, 28  
 Kertecz, 182, 217  
 Kettner, 15  
 Kielleuthner, 308  
 Kienbock, R., 24, 74  
 Killian, 17, 25  
 Kimura, 445  
 Kirchheim, 103  
 Kirschner, 449  
 Kirschner, M. and Mangold, E., 43  
 Kirschstein, 228  
 Kistler, 384  
 Klapp, 168  
 Klauber, 220, 258  
 Klauser, 314, 389  
 Klebs, Edwin, 12, 76  
 Klebs and Welt, 474  
 Klecki, 258, 304  
 Klee, P., 43, 44, 46  
 Klee, P. and Klupfel, O., 126, 136  
 Klein, 256, 449  
 Kleinschmidt, 313, 395  
 Kleist and Forster, 315  
 Klemperer, 463  
 Klippel, 439  
 Klopstock, 121  
 Klose, 342, 350, 351  
 Klose, H. and Vogt, H., 152, 352, 353, 406  
 Klug, 68  
 Knape, W., 100, 103  
 Knapp, 220, 253  
 Knoll, 285  
 Kobayaski, M., 76  
 Koch, 463  
 Koch, W., 134, 178, 298, 304, 307, 309,  
     338, 463  
 Koch and Filehne, 412, 413

- Kocher, 175, 214, 217, 218, 223, 225, 329, 338, 340, 342, 344, 347, 348, 403, 410, 411, 413, 420, 421, 460, 468
- Kocher, A., 56, 63, 79
- Kocher and Prutz, 223
- Kocher, Thomas, 80, 363
- Koehler, 389
- Koenig, 323
- Koerte, 238
- Koerter, 238
- Kohler, 389
- Kohnstamm, 1
- Kohts, 381
- Kolb, 366 (ref. 402), 455
- Kolle and Otto, 463
- Kolliker, 459
- Kolozoff and Brunn, 161
- Kon, 157
- Kondolean, 482
- Konen, 458
- Konig, 440, 443, 447, 448, 449, 454
- Konig and Paschen, 466, 469
- Konjetzny, 207
- Koranyi, 281, 288
- Korber, 411
- Korte, W., 52, 104, 138
- Korteweg, 429
- Kostel, 345
- Kottmann, 341
- Krabbel, 363
- Krabbel, M. and Gleinitz, H., 79
- Kragelund, 448, 449
- Krall, 358
- Kramer, 310, 311, 412
- Krapp, 9
- Kraske, 179, 450
- Krasnogorski, 70
- Kraus, 12, 23, 24, 463
- Kraus, Fr., 346, 349
- Kraus and Friedenthal, 348, 350
- Krause, Fedor, 57
- Krauss, 438
- Krehl, Ludolf, 24, 50, 130, 477
- Krehl and Marchand, 372
- Kreidl, 362
- Kremer, 437, 439
- Krempelhuber, M., 54
- Kretz, 79, 128, 129, 133, 257
- Kreuter, 149, 151
- Krogh, 372
- Krogins, 242
- Kroh, 447, 450, 451, 452, 464
- Kroher, 251, 253
- Krohnlein, 412
- Kroiss, 12, 13
- Kron, 434
- Kronecker and Meltzer, 15, 16, 19, 21, 24
- Kronecker and Schmey, 365 (ref. 402)
- Kronig and Gauss, 406
- Kronlein, 403, 412
- Kruger, 456
- Kubig, G., 140
- Kuhn, 96, 388, 481
- Kuhne and Lea, 96, 100
- Kukula, 225, 264, 266
- Kumita, 314
- Kummell, 28, 65, 291, 293, 295, 307
- Kunika, 131
- Kuru, 52
- Kushimura, 472
- Kusmine, 125
- Kussmaul, 53, 361
- Kussmaul and Tenner, 417, 419
- Kuster, 295, 299, 308
- Kutschera, 342, 343, 345
- Kuttner, Hermann, 6, 56, 74, 79, 148, 152, 160, 167, 312, 394, 403, 435, 453, 455, 469
- Kuttner and Landois, 435, 436
- Laennec, 448
- Laewen, 333, 366 (ref. 402)
- Laguesse, E., 100
- Laimer, Monro, 26
- Landau, 299
- Landau, M. and McNee, J. W., 300
- Landois, 287, 359, 419, 435, 474
- Lane, 211, 448
- Lange, 119, 355, 437
- Langemaak, 296
- Langemak, 13, 295, 468
- Langenbecks, 469
- Langenbuch, 118, 120
- Langendorff, 97, 381
- Langendorff and Mommsen, 314
- Langerhans, R., 101, 102
- Langley, 6, 171
- Langley, J. N., 43, 314
- Langley and Magnus, 194, 197
- Langmak, 296
- Lannelogue, 461
- Lanz, 180, 256, 341, 346, 363, 364, 482

- Larguier des Bancels, 97  
 Larrey, 365  
 Larroche, 132  
 Latarjet, A. and Cade, A., 81  
 Lattler, 346  
 Latzko, 292  
 Laubenheimer, 134  
 Laudenbach, 152  
 Lauenstein, 220  
 Lawen and Sievers, 389, 391  
 Lawson, and Tait and Heidenhain and Vogel, 162  
 Lebedeff, 113  
 Leber, 462  
 Ledderhose, 164, 378, 468, 471  
 Legg, 438  
 Leggett, N. B. and Maury, J. W. D., 56  
 Leguen, 52  
 Lehmann, G., 78, 433  
 Leichtenstern, 213  
 Lendorf, 321, 322  
 Lengemann, 395  
 Lenk, 298  
 Lennander, K. G., 47, 162, 172, 283, 291, 436  
 Lennander and Nystrom, 242  
 Lennander and Wilms, 172  
 Lenormant, 269  
 Lepehne, G., 151, 153  
 Lepine and Barral, 97  
 Leporski, 366 (ref. 402)  
 Lequen, 277  
 Leriche, R., 1  
 Leser, 450  
 Lesser, 472  
 Lesshaft, 447  
 Letienne and Hanot, 124  
 Letulle, 74  
 Leube, 6, 297, 319  
 Leueberger, 319  
 Leuenberger, 228, 319  
 Leverenz and Schoenwerth, 160  
 Levi and Ludloff, 455  
 Levy, R., 9  
 Lewandowsky, 171, 404, 459  
 Lewin, 127, 307  
 Lewin and Goldschmidt, 301, 303, 310  
 Lewis, 365 (ref. 402)  
 Lexer, 393, 461, 467, 469  
 Lexer and Kuliga and Turk, 461  
 Leyden, 407  
 Lichtenbelt, J. W., 76  
 Lichtenberg, 248, 301, 395, 396, 397  
 Lichtenstern, 324  
 Lichtheim, 372, 378, 381, 386  
 Lichtwitz, L., 132, 313  
 Licini, C., 70, 77  
 Liebermeister, 129  
 Lieblein, 148  
 Lieblein, V., 265  
 Liek, 292, 293, 455  
 Lindemann, 288, 289, 395  
 Linser, 407, 473  
 Lintbeck, 287, 288  
 Lissauer, 117, 119, 121, 124, 128  
 Litten, 233  
 Litthauer, 77  
 Lob, 474, 475  
 Lobenhofer, 282, 293, 344  
 Loeb, A., 125, 311  
 Loeschke, 322, 323, 388  
 Lohmann and Muller, 379, 388  
 Lombroso, U., 99, 100, 101  
 London, 265  
 Longuet, 230  
 Looser, E., 135  
 Lorenz, 220, 429, 445  
 Lorin, 302  
 Lossen, 217, 218  
 Lovett, 438  
 Lowenstein, 470  
 Lowit, 395  
 Lubarsch, 121  
 Luciani, 4, 154, 428, 429, 433  
 Lucke, 443, 460  
 Luckhardt, A. B. and Henn, S. C. and Palmer, W. L., 96  
 Ludakeevitsch, 153  
 Ludloff, 267, 268, 269, 449  
 Ludsucki, 389  
 Ludwig, 1, 280  
 Luscher, 20  
 Luschka, 199  
 Lusk, Graham, 115  
 Luter, 284  
 Luthi, 338  
 Maas, 295, 435  
 Maas and Pinner, 318  
 Macleod, J. J. R., 37  
 Madelung, 328  
 Mafucci, 167



- Magendie, 19, 405  
 Magendie and Longet, 18  
 Magnan, 418  
 Magnus and Alsleben, 119, 225, 226  
 Magnus and Levy, 342, 346, 348  
 Magnus, R., 43, 97, 127, 194, 373, 435,  
     446, 463  
 Malassez and Ponchet, 155  
 Malchol, 454  
 Malcolm, 229  
 Mall, 170  
 Manasse, 50  
 Manfredi, 480  
 Mangold, E., 52, 65  
 Mann, 229  
 Mansfeld and Muller, Fr., 346  
 Manteuffel, 213  
 Maragliano, D., 105  
 Marburg and Ranzi, 416, 422  
 Marchand, 54, 161, 364, 395, 435, 472  
 Marchand and Krehlschen, 165  
 Marckwald, 17  
 Marcus, 303, 306, 307, 310  
 Marek, 234  
 Marey, 429, 476  
 Marine, D. and Kimball, O. P. and  
     Rogoff, J. M., 347  
 Marinesco and Minea, 341  
 Marion, 322  
 Martens, 448  
 Martin, 435  
 Martin, Sidney and Dawson, 127  
 Martini, 292  
 Martius, F., 77, 78  
 Marwedel, 461  
 Marzocchi and Bizzozero, 13  
 Masius, 283  
 Massland, 413  
 Mathieu, 209  
 Mathieu, A. and Roux, J. C., 53  
 Mathiew, A. and Savignac, R., 61  
 Mathiew and Roger, 59  
 Matsuoka, 329  
 Matthes, M., 54, 60, 62, 66, 69, 233  
 Matti, 201, 351, 356, 392, 427, 431, 455  
 Mauthner and Pick, 229  
 Maximore, 6  
 May, W. P., 44  
 Maydl, 222  
 Mayer, Aug., 180  
 Mayer, Fritz, 74  
 Mayer and Gottlieb, 5, 9  
 Mayersbach, 457  
 Mayo, W. J., 63  
 Mayo-Robson, 124, 126, 135  
 McCallum, 359, 363, 364  
 McCosh, 233  
 McLean, 227, 259  
 McMaster, P. D. and Rous, P., 128  
 McNee, J. W., 128, 132  
 Meaugedis, 295  
 Meckel and Helmsbach, 131  
 Medwedew, 363  
 Meinert, 360, 361  
 Meinertz, 308  
 Meisel, 170, 241, 245, 256, 258, 416  
 Melchior, 326, 328, 346, 354  
 Melchior and Loser, 263  
 Melchior and Suter, A. O., 318  
 Melnikow and Montuori, 154  
 Meltzer, 16, 17, 21, 137  
 Menge, 293  
 Menzels, 441  
 Mering, 64, 95, 98  
 Mering and Aldehoff, 40, 44, 49  
 Merkel, 72  
 Merrem, 64  
 Merten, 412  
 Merzbacher, 202, 208  
 Messerer, 411, 413, 421  
 Mestrezet, 404  
 Metschnikoff, 168, 245, 246  
 Metzger, 152  
 Metzner, 314  
 Meyer, A. W., 148, 151, 152, 154, 155, 173,  
     414  
 Meyer and Betz and Gebhardt, 202  
 Meyer and Gottlieb, 171  
 Meyer, H., 428  
 Meyer and Jungmann, 282, 283, 284  
 Meyer, O. B., 314  
 Meyer, R., 181  
 Michaelis, 366 (ref. 402)  
 Michaud, 421  
 Miflet, 328  
 Mikulicz 21, 22, 25, 27, 251, 452  
 Miller, Fr., 192  
 Miloslavich and Namba, 262  
 Minkowski, 98, 125, 129, 372, 375, 378  
 Minkowski and Naunyn, 128  
 Mobius, 346, 347  
 Mocckel, 420

- Moeckel, K. and Rost, F., 97  
 Mohr, 7, 9  
 Molitoris, 365 (ref. 402)  
 Moll, 442  
 Moller, 361  
 Molnar, 191  
 Momburg, 419  
 Monakow, 281  
 Monari and Umberto, 66, 265, 266, 267  
 Monckeberg, 162, 364  
 Monroe, 26, 448  
 Monroe, 407  
 Mora, Henri, 101  
 Morandi and Sisto, 151  
 Morano, G. P. and Baccarani, W., 7  
 Morawitz, 115  
 Morawitz, P. and Bierich, 130  
 Morawitz and Siebeck, 441  
 Morgagni, 18, 230, 365  
 Moricke, 9  
 Morison, 179  
 Moritz, 181, 182  
 Moro, 185, 362  
 Morpurgo, 287  
 Morris, 253  
 Mosengeil, 464, 465  
 Moskowitz, 246  
 Mosler, 152  
 Mosse, 157  
 Mosso, 430, 439  
 Most, 464, 480  
 Motschutkowsky, 423  
 Moty, 230  
 Mouton, 30  
 Moynihan, 263  
 Muck, 478, 479  
 Muhsam, R., 157, 196, 257  
 Muller, 8, 71, 205, 292, 314, 316, 465, 466  
 Muller, Albert, 37, 47, 195, 307, 314  
 Muller, Fr., 101, 281, 284, 287, 303, 358  
 Muller, Johannes, 40, 434  
 Muller, L. R., 43, 66, 174, 175, 201, 208  
 Muller, P., 53  
 Mummery, 229  
 Munk, 127, 417  
 Muralt, 384  
 Murphy, 467  
 Muscatello, 161, 167  
 Musculus, 319  
 Myers, 134  
 Mylard, 254  
 Naegeli, 150, 354, 361  
 Nagamori and Hikohachi, 76  
 Nagano, 266, 267, 321  
 Nakahara, 297  
 Nakahara and Dilger, 454  
 Narath, II, 116, 192, 215  
 Narath, II, 116, 117  
 Narath, II and Steckelmacher, S., 117  
 Nasse, 130, 136  
 Natus, M., 100, 101, 103  
 Naumann, 132  
 Naunyn, 124, 131, 165  
 Naunyn and Schreiber and Falkenheim,  
     403, 405, 407  
 Nauwerck, C., 74  
 Nauwerk, C. and Lubke, 139  
 Neisser, 242  
 Neisser and Wechsberg, 463  
 Nelaton, 164  
 Nencki and Pawlow, 112  
 Nepper, 127  
 Nesbieth, 225  
 Neu and Hermann, 405  
 Neuber, 364  
 Neugebauer, 24, 452  
 Neuhaus, 63, 464  
 Neuhaus and Hildebrand, 56, 464  
 Neumann, 172, 220  
 Neumann, A., 232  
 Neumann, E., 69, 74  
 Neumann, R., 233  
 Newton, 421  
 Nicol, 8  
 Nicoladoni, 181  
 Nicolletti, 116  
 Niebergall, 478  
 Niederstein, 234  
 Nigrisoli, 264, 266  
 Nikolaysen, 225  
 Nissen, 355  
 Nitsche, E., 73  
 Nobl, 469  
 Nocard, 305  
 Noetzel, 251  
 Noguchi, 463  
 Nolf, P., 116  
 Nonne, 409, 482  
 Nonne and Apelt, 405  
 Nordmann, 351  
 Nothnagel, 173, 174, 176, 194, 212, 223,  
     250, 253, 417, 437, 477

- Notkin, 339  
 Notzel, W., 140, 149, 166, 183, 244, 397,  
     398, 463, 465, 480  
 Nowatski and Arndt, 420  
 Nussbaum, 251  
 Nystrom, 242, 436  
  
 Oberdorfer, 262  
 Oberndorffer, 23  
 Oddi, 126, 136  
 Oehlecker, 321  
 Offergeld, 396  
 Ogata, M., 67  
 Ohlecker, 176  
 Ollier, 435, 469  
 Olshausen, 216  
 Openchowski, 22, 43, 45  
 Opitz, 304  
 Oppenheim, 96, 224, 415, 447  
 Oppenheim and Locw, 311  
 Oppenheimer, 97, 319  
 Oppler, 203  
 Ore, 122  
 Orfila, 318  
 Orlow and Heidenhain, 168  
 Orth, Johannes, 9, 73, 308  
 Orthmann, 463  
 Ortner, 174  
 Orzechowski, 362, 416  
 Osborne, T. B. and Mendel, L. B. and  
     Ferry, E. L., 312  
 Oser and Pribram, 154  
 Osthoff, 288  
 Ostwald, Adolph, 124  
 Oswald, 338, 346, 348  
 Otto, E., 40  
  
 Pagenstecher, 164, 166, 464  
 Paget, 449  
 Paine, 257  
 Pal, 170  
 Palmer, W. W. and Van Slyke, D. D., 291  
 Paltauf, 23, 355, 364  
 Pansini, 242, 247  
 Panum, 72  
 Parlavecchio, 292  
 Partsch, 458  
 Passavant, 16  
 Passler, 348  
 Passler and Heinecke, 286  
 Passow, 363  
  
 Pasteur, 462  
 Paterson, 264  
 Patrimon, 62  
 Pauchet, 264, 266  
 Pavy, 71  
 Pawlow and Boldireff, V. N., 39  
 Pawlow, I., 2, 11, 41, 43, 47, 49, 59, 95,  
     96, 97, 126, 135  
 Pawlow, J. P. and Schumowa-Siman-  
     owskaju, 43, 49  
 Pawlowski, 243  
 Payr, 72, 73, 162, 180, 237, 253, 254, 263,  
     393, 408, 434, 464, 465, 467, 468, 469  
 Payr, A. and Martina, E., 104  
 Pean, 64  
 Pearce, 286  
 Pearce, R. M. and Krumbhaar, E. B. and  
     Frazier, C. H., 149  
 Peiser, 167, 169, 243, 245  
 Pels, Leusden, 309  
 Pelschinsky, 13  
 Pennington, 207, 230  
 Penzoldt, 163  
 Peres, 148  
 Perez, 154, 464  
 Peritz, 362, 364  
 Pernice and Scagliosi, 304  
 Perrier and Hartmann and Monprofit, 55  
 Perthes, G., 65, 207, 248, 384, 422, 441,  
     458  
 Petersen, Walther, 37, 59, 60, 380  
 Petren, 30  
 Petry, 231, 232  
 Pettavel, 351  
 Pfaff and Balde, 125  
 Pfaundler, 285  
 Pfeifer, 314  
 Pfeiffer, 348  
 Pfeiffer and Kolle, 244  
 Pfeiffer, R., 247, 287, 289  
 Pfeiffer and Wassermann, 247  
 Pflanz, 209  
 Pflaumer, 282, 284 315  
 Pfluger, 111  
 Phleps, 359  
 Pick, 129, 255  
 Piktin, 153  
 Pinkus, 208  
 Piorry, 436  
 Pirogoff, 412  
 Pirone, 178, 179

- Placzek, 365 (ref. 402)  
 Plaschke, S. and Schur, H., 80  
 Pletnew, 125  
 Pochhammer, 454, 459  
 Pohl, 155  
 Poirier, 277  
 Poly, E., 103  
 Pommer, 214, 445  
 Poncet, 449  
 Ponfick, 110, 285, 301  
 Popielski, L., 2, 41, 43, 44, 95, 96, 97, 155, 172  
 Popper, 352, 458  
 Poppert, 395  
 Porter, 366 (ref. 402)  
 Posner, 297, 301, 305, 313, 314, 316, 320, 329  
 Posner and Lewin, 306  
 Preiser, 446, 447  
 Pretsch, 181  
 Prettin and Leibkind, 389  
 Pribram, 373  
 Primbs, 302  
 Propping, 172, 220, 251, 252, 253, 379, 406  
 Propping and Dieterichs, 220  
 Prutz, 233  
 Prutz and Ellinger, 196  
 Purkhauer, 432  
  
 Quarta, 154  
 Quenu, 458, 476  
 Quenu and Hartmann, 207  
 Quenu and Walter and Routier, 277  
 Quervain, 222, 339  
 Quincke, 120, 123, 130, 138, 284, 314, 404, 406, 415  
 Quincke, H. and Dettweiler, 77  
 Qurin, 224  
  
 Rabe, 124  
 Raiser, 197  
 Ramstroem, 176  
 Ranke, 217  
 Ransohoff, I., 120  
 Ranzi and Tandler, 351  
 Ranzier, 14  
 Rashford and Southgate, 127  
 Rautenberg, 301, 302  
 Ray and Sherrington, 410  
 Raymond, 438  
 Reach, F., 126  
  
 Real, 450  
 Recklingshausen, 72, 167, 234, 391, 477  
 Redlich, 362, 416  
 Redlich and Binswanger, 416, 418  
 Redwitz, 65, 72, 79, 210, 261  
 Reerink, 322  
 Regnier, 441, 442  
 Rehfish, 314, 317, 321  
 Rehn, 251, 252, 255, 319, 351, 365 (ref. 402), 468  
 Reich, 24, 434  
 Reich and Blauel, 346  
 Reichard, 73  
 Reichardt, 403, 408, 409  
 Reichel, 192, 215, 228, 243  
 Reichmann, M., 54, 406  
 Reifs, 287  
 Reimann, S. P. and Bloom, G. H. and Reimann, H. A., 378  
 Reineboth, 374, 382, 384  
 Reiner, 392, 393  
 Reiniger, Clara, 135  
 Reinsbach, 482  
 Remak, 481  
 Renner, 282, 283  
 Renton, 458  
 Retzius, 22  
 Reyher, 442  
 Rheinbolt, M., 49  
 Ribbert, 71, 119, 257, 389, 391, 392, 472  
 Ribbert and Kruse and Fischer, B., 465  
 Richards, A. N., 280  
 Richet, Ch., 81, 154  
 Ricker, G., 103, 104, 298  
 Riedel, 101, 137, 164, 181, 205, 256, 263, 300, 392, 464, 476  
 Rieder, 36, 194, 197  
 Riedinger, 442  
 Riegel, 365 (ref. 402)  
 Riegner, 152, 155  
 Rimann, 448  
 Rio Branco, 116  
 Rippert, 262, 304  
 Risel, 140, 391  
 Ritter, 293, 355, 480  
 Ritter, A., 73  
 Ritters, 444  
 Riva-Rocci, 278  
 Rivington, 320  
 Rivinus, 177  
 Rjesanoff, 210



- Robinson, 255, 383, 384  
 Robson, Mayo, 124, 126, 135  
 Rochet, 319  
 Rockwitz, C., 60  
 Rodet, 461  
 Roessle, 76, 350  
 Roger, 127, 178, 226, 461  
 Rogoszinsky, 305  
 Rogowitsch, 341  
 Rohde and Ellinger, 282, 285, 379  
 Rohleder, 325  
 Rohr, 242  
 Rohrbach, 407  
 Roith, 193, 254  
 Rokitansky, 253  
 Rolando, 13  
 Rolly, 308  
 Romanoff, 380  
 Romberg and Passler, 248  
 Romer, 462  
 Ropke, 463  
 Rose, 21, 365 (ref. 402)  
 Rosenbach, 104, 372, 375, 384, 385, 460  
 Rosenbach and Schschterbak, 421  
 Rosenbaum, 18  
 Rosenberg, 97, 99, 100, 125, 127, 136  
 Rosenheim, 23, 254  
 Rosenow, E. C., 75  
 Rosenstein, P., 119, 122, 180  
 Rosenthal, 375  
 Roser, 178, 217, 384, 385, 445, 460, 467  
 Rosler, 77  
 Rossolino, 207  
 Rost, F., 2, 6, 8, 19, 29, 58, 105, 123, 125, 126, 136, 140, 154, 178, 179, 193, 207, 209, 210, 221, 222, 223, 253, 267, 301, 302, 314, 317, 321, 322, 357, 451, 457, 463, 466, 472, 474, 481  
 Rotschild, 322  
 Rotter, 251, 252, 253  
 Roubaix, 218  
 Roubitschek, 305, 306  
 Rouotte, 123  
 Rous, P. and McMaster, P. D., 137, 139  
 Roussi and Rossi, 201  
 Roux, 427, 429, 440, 441  
 Roux, J. C. and Riva, A., 68  
 Roux and Roger and Sosne, 257  
 Rouxeau, 359  
 Rovsing 184, 185, 293, 310, 318  
 Rovsing and Niels and Thorkild, 54  
 Roy, 28, 155  
 Roy and Sherrington, 410  
 Rubaschow, S., 140  
 Rubin, 179  
 Rudinger, 341, 359, 360, 361  
 Ruge, 291, 293, 294, 301  
 Rumpf, 421  
 Runeberg, 240, 256  
 Runge, 322  
 Rutimeyer, 78  
 Ruttermann, 9  
 Rydigier, 236, 481  
 Rywosch, 130  
 Saar, 380, 381  
 Sabrazes, J. and Faguet, C., 8  
 Sachs, 97  
 Sackur, 379, 381  
 Sagimura, 305  
 Sahli, 478  
 Saito, 463  
 Sakata, 305  
 Salis, 347, 388  
 Salis and Vogel, 347  
 Salkowski, E., 5, 6, 468  
 Salou, 96  
 Samuel, 461  
 Sanarelli, G., 3  
 Sarbach, 340  
 Sasse, F., 66  
 Sattler, 349  
 Sauerbruch, 25, 227, 230, 232, 351, 359, 365 (ref. 402), 372, 373, 375, 376, 379, 380, 382, 383, 384, 386, 403, 407, 413, 419  
 Sauerbruch and Haecker, 23, 24  
 Sauerbruch and Heyde, 287  
 Savo, 307  
 Sawamura, 309  
 Scarpa, 185  
 Schablowsky, 465  
 Schade, H., 11, 12, 131, 132, 313  
 Schall, 389  
 Schambacher, 470  
 Schanz, 443  
 Schattenfroh, 246  
 Schatz, 181, 183  
 Schede, 384  
 Scheidemantel, 304  
 Scheidtmann, 253  
 Scheier, 15

- Schenker, 388  
 Schepelmann, 386, 468  
 Schepowalnickow, 191  
 Scheuerlen, 463  
 Schiefferdecker, 176, 177, 180  
 Schiesselbein and Ritter, 139  
 Schiff, 18, 24, 76, 122, 125  
 Schiff and Contejean, 41  
 Schiff and Zack, 438, 439  
 Schifferdecker, 422  
 Schifone, 415  
 Schischko, 302  
 Schittenhelm and Weichardt, 204, 344  
 Schlagenhauer and Wagner and Jouregg,  
     342, 344  
 Schlagintweit, E. and Stepp, W., 96  
 Schlange, 322, 323, 324  
 Schlatter, C., 67  
 Schlayer, 281, 289  
 Schlesinger, 383, 395  
 Schlesinger, E., 56, 210  
 Schlesinger, W., 97, 222  
 Schlossman, 453, 458  
 Schloffer, 236  
 Schmaus, 421  
 Schmerz, 468  
 Schmid, 17, 171  
 Schmidt, 18, 165, 202, 217, 364, 481  
 Schmidt, A., 97, 101, 191, 192, 206  
 Schmidt, Ad. and Strassburger, 203  
 Schmidt and Aschoff, 307  
 Schmidt, G. B., 436  
 Schmidt and Lohrisch, 210  
 Schmidt, Mulheim, 165  
 Schmidt, J. E. and Betke, 329, 364  
 Schmidt, J. H., 47  
 Schmidt, M. B., 153, 469  
 Schmieden, V., 241, 297, 450, 469  
 Schmincke, 148, 154  
 Schmorl, 337  
 Schmorl and Ingier, 356, 392, 405, 463  
 Schneider, 363  
 Schnitzler and Ewald, 167, 169  
 Schoemaker, T., 56, 58  
 Schoenfeld, 154  
 Schonborn, 348  
 Schoppe, 458  
 Schott, 178  
 Schottmuller, 10  
 Schrader, 170, 247  
 Schramm, 5  
 Schreiber, 15, 21, 182, 293, 474  
 Schroder, 112, 135  
 Schrottenbach, 415  
 Schruppf, 256  
 Schrunder, 162, 166  
 Schuchardt, 68  
 Schuller, L., 38, 55, 56, 59, 61, 64  
 Schulten, 15  
 Schultz, 476  
 Schultze, 463  
 Schultze, F., 149  
 Schultze, W., 104  
 Schulz, Emma, 185  
 Schulze, 100, 348  
 Schumm, 96  
 Schupbach, 127  
 Schuppel, 119  
 Schuster, 366 (ref. 402)  
 Schutz, R., 203  
 Schwalbe, 473  
 Schwartz, 285, 314, 317  
 Schwarz, G., 17, 37, 79, 194, 197, 200,  
     209  
 Schwarz, K., 79  
 Schwenkenbecker, 20  
 Scott, R. W., 303, 377  
 Seelig and Lyon, 229  
 Seeliger, 308  
 Segale, 318, 467  
 Seggel, 449  
 Seidel, H., 105, 135, 298, 383, 388  
 Selter, 305  
 Senator, 297  
 Seringer, 56  
 Sherington, 432  
 Shimodeira, 223  
 Shingu, 384  
 Short, 230  
 Shulten, 15  
 Sick, 139, 225, 264  
 Siebeck, 375, 386  
 Sievers, 390  
 Silbermann, O., 77, 474  
 Silhol, 764  
 Simmonds, Morris, 37, 105, 296, 310, 312,  
     328  
 Simon, 296  
 Singer, 209  
 Singer, C., 74  
 Singer, G., 76  
 Sinnhuber, 24

- Sittmann, 304  
 Sjubimowa, 75  
 Skzreczka, 375  
 Smirnow, 282, 283  
 Snel, 396  
 Soli, U., 351  
 Solowieff, 118  
 Sonnenburg, 54, 256, 260, 261, 262  
 Soulie, 155  
 Soyesima, 265, 266  
 Spalteholtz, 17, 365, 476  
 Spemann, 457  
 Spiess, 459  
 Spitz, 457  
 Sprengel, O., 72, 234, 238, 239, 247, 249,  
     255, 256, 259, 260, 262  
 Ssolowjeff, 67  
 Stadelmann, 125, 128, 129  
 Stadler, 224  
 Stachelin, 372, 381  
 Stark, 23, 24, 25  
 Starlin, 194  
 Starling and Bayliss, 95  
 Starling and Tubby, 168  
 Stasoff, 266  
 Stawraky, W., 99  
 Steenhuis, 118  
 Steinach, 325, 329  
 Steiner, 138, 329, 456  
 Steinert, 456  
 Steinharter, E. C., 74  
 Steinlein, 341  
 Stempel, 446, 453  
 Stern, R., 162, 247, 398  
 Sternberg, 482  
 Steudel, 59  
 Stewart, 305  
 Stewart and Barbes, 302  
 Steyrer, 285  
 Sthamer, E., 72  
 Stich, 474, 478  
 Stier, 441  
 Stierlin, E., 65, 194, 202, 209, 211  
 Stierlin and Rieder, 198  
 Stiller, 36, 53, 78, 184, 299, 329  
 Stiller and Glenard, 208  
 Stilling, 329  
 Stintzing, 459  
 Stoeber and Dahl, 257  
 Stoerk, 297  
 Stoffel, 422, 457  
 Stovesand, 375  
 Strangury, 379, 383  
 Strassburger, 202, 203  
 Strasser, 438, 444  
 Strassmann, 303  
 Straub, 289  
 Straup, 206  
 Strauss, 200, 287, 318, 319  
 Strauss and Gernout, 301  
 Strehl, 172, 248, 249  
 Stricker, 5  
 Strohmeyer, F., 74, 412  
 Strubell, 294  
 Strumpell and Vulpian, 438  
 Stuber, 59, 71  
 Stuberauch, 136, 151, 320  
 Studensky, 313  
 Stursberg, 292, 395  
 Sturtz, 373, 386  
 Sturtz and Sauerbruch, 209  
 Stutzer, 178  
 Sudeck, 436, 440, 453, 454  
 Sultan, 13, 220  
 Sulzer, 438, 439  
 Sumita, 368, 467  
 Suter, 307  
 Suzuki, T., 178  
 Svehla, 352  
 Swanson, 7  
 Sweet, J. E., 105, 228  
 Szymanowski, 19  
 Takoyusu, 265  
 Talke, 475  
 Talma, S., 47, 75, 122, 215  
 Tandler, 328  
 Tandler and Gross, 324, 325  
 Tappeiner, 117, 119, 125, 467  
 Tarulli and Pascucci, 154  
 Tashiro, 445  
 Tavel, E., 58, 59, 60  
 Tavel and Lanz, 243, 256, 257  
 Teevan, 411  
 Teleky, 437  
 Telemann, 22, 27  
 Tendeloo, 309, 374, 380  
 Ten Horn, 257  
 Tenner, 417  
 Terrier, 277  
 Teutschlander, 311, 392  
 Thaler, 360

- Thelemann, 292  
 Thiery, 14, 17, 190  
 Thiesssch, 384  
 Thoele, 111  
 Thole, 116, 119, 421  
 Thoma, E., 66  
 Thommen, 230  
 Thorspecken, 124  
 Thran, 119  
 Tiedemann, 152  
 Tiegel, 383, 384, 394  
 Tietze, Allen, 62  
 Tigerstedt, 378  
 Tigerstedt and Bergmann, 289  
 Tillmann, 24, 122, 295, 397, 411, 413, 437, 464  
 Tilmann and Bungart, 418, 420, 439  
 Tischner, 130  
 Tizzoni, 151, 152, 155  
 Tobler, L., 40, 41, 42  
 Toldt, 199  
 Tomsa, 328  
 Torek, 253  
 Trager, 268  
 Trappe, 453  
 Traube, 288, 372, 381  
 Treindlsberger and Schlagintweit, 312  
 Trendelenberg, 194, 238, 339, 389, 460, 471, 475  
 Treskin, 318  
 Trinkler, N., 66  
 Tromberg, 392, 393  
 Tronyl, 1  
 Trouseau, 360  
 Trouseau and Leblanc, 163  
 Trzebicki, 265, 266, 267  
 Tschekunow, J. S., 42  
 Tsunoda, T., 130  
 Tuffier, 52, 301  
 Tuffier and Ehrhardt, 292  
 Tuffier and Rosenbach, 314  
 Turck, F. B., 74  
 Turk, 157  
 Uffenheimer, A., 42  
 Ujeno, 161  
 Ullmann, 320  
 Umber, 42  
 Umbreit, 119  
 Unger, E., 66, 291  
 Ury, 192, 203  
 Uskoff, 463  
 Uxkull, 430  
 Van Braam and Honckgeest, 44  
 Van de Kamp, 394  
 Van Roojen, P. H., 61  
 Van Slyke, 112, 290  
 Vanghetti and Sauerbruch, 434  
 Vaquez, 475  
 Vassale, 360, 363  
 Vassale and Generali, 359  
 Vazin, 439  
 Veil, 285, 286  
 Venus, 398  
 Verlicae, 293  
 Verneull, 269, 476  
 Verse, 118, 133  
 Verth, 478  
 Viborg, 13  
 Vignolo, 478  
 Vincent, 338  
 Viola, 480  
 Viola and Gaspardi, 70  
 Virchow, 8, 22, 70, 234, 253, 388, 391, 392, 414, 473  
 Virgli, 321  
 Voelecker, 244, 251, 303, 310, 452, 454  
 Vogel, H., 148, 161, 162, 277, 347  
 Vogt, 459  
 Voisin and Petit, 419  
 Volcker, 301, 474  
 Volhard, 279, 281, 282, 287, 288, 292  
 Volkman, 429, 435, 440, 442, 445, 450, 451, 459, 460, 465  
 Von Bramann, 13  
 Von Eiselberg, 20  
 Vulpian, 439, 440, 441  
 Vulpian, 148, 149, 152, 154  
 Wagner, 8, 9, 11  
 Wahl, 413, 478, 479  
 Walbaum, 249  
 Waldeyer, 267, 460  
 Waldeyer and Volckmann, 460  
 Wolkoff and Delitzin, 299  
 Walkhoff and Ewald and Preiser, 445, 447  
 Wallgreen, 244  
 Wallney, 320  
 Walthard, 243  
 Walther, F. K., 97, 341  
 Walther and Hosemann, 348



- Walz, 356  
 Wasserthal and Epstein, 305, 306  
 Wassilief, 19  
 Wearn, J. T., 280  
 Weber, E. F., 428, 429, 443  
 Weber, O., 392, 476  
 Weber, Th., 478  
 Wegner, 166, 170  
 Wehrmann, C., 4  
 Weichselbaum, A., 99, 445, 448  
 Weidenreich, 178  
 Weil, 15, 169, 239  
 Weinland, 190, 240  
 Weintraud, 124  
 Weisker, 181  
 Weiss, 222  
 Weissgerber, 384  
 Weissgerber and Perls, 293  
 Weitz, 385  
 Wells, 251, 289  
 Wendel, 23, 415  
 Wendelstadt, 346  
 Wendt, E. C., 8  
 Wenkebach, 373  
 Wenzel, 269  
 Wertheim, 479  
 Werzejewski, 392  
 West, 374  
 Westphal, 417  
 Westphal, K. and Katsch, 76, 77  
 Wettstein, 56  
 Wheelon, H. and Thomas, J. E., 40, 46  
 Whipple, G. H. and Sperry, J. A., 114, 228  
 Wickmann, 362  
 Widmer, 24  
 Wiebrecht, 363  
 Wiedemann, 138  
 Wiedhopf, 183, 185  
 Wieland, 254  
 Wiener, 363  
 Wiesel, 354, 355, 356  
 Wieting, 478  
 Wilbrand and Sanger, 410  
 Wildboltz, 284, 309, 310  
 Wilkie, D. P. D., 54, 64  
 Wilms, M., 50, 75, 98, 135, 175, 209, 212,  
     216, 220, 228, 235, 238, 253, 260,  
     283, 300, 323, 344, 388, 404, 420, 421,  
     454, 455, 459  
 Wilms and Posner, 324  
 Windboltz, 296  
 Winiwarer, 64, 481  
 Winkler, 152, 257  
 Winternitz, M. C. and Smith G. H. and  
     Robinson, E. S., 396  
 Wirth, 359, 361  
 Witzel, 177  
 Wohlgenuth, J., 96, 97, 112, 113, 124, 126  
 Wolf, 394, 395  
 Wolff, 295, 296, 428, 430  
 Wolff, A., 22  
 Wolff, J., 428  
 Wolfer, A., 59  
 Wollenburg, 445, 446, 447, 448  
 Wossidlo, 296, 303  
 Wrede, 435  
 Wreden, 306  
 Wright, 475  
 Wroblewski, 67  
 Wunderlich, 298  
 Wundt, 434  
 Wunschheim, 307  
 Wurster, 307, 334  
 Wurttemberg and Altbuerg, 312  
 Wurtz, R. and Lendet, R., 74  
 Yanase, 362  
 Yatsushiro, T., 73  
 Zadyier, 292  
 Zagari, 6  
 Zahn, 118, 472, 473, 474  
 Zahn and Chandler, 165  
 Zander, 381  
 Zangemeister, 288  
 Zehnder, 480  
 Zeidler, 277  
 Zeissl, 314  
 Zencker, 20, 29, 393, 435, 437  
 Zesas, D. G., 152, 241, 355, 380, 381  
 Ziegenspeck, 269  
 Ziegler, 156, 161, 445  
 Ziehen, 417  
 Ziemssen, 25, 29, 474  
 Ziesch, 266  
 Zietzschmann, 341  
 Zigerus, 177  
 Zimmermann, 14, 20, 27, 175, 316  
 Zollner, 317  
 Zondek, 292, 293  
 Zuckerkindl, 262, 268, 316, 322  
 Zuntz, 477  
 Zuntz and Tacke, 213  
 Zuppinger, and Christen, 431  
 Zurhelle, 473



## SUBJECT INDEX

---

- Abdomen, 161; and pain, 173; pendulous, 183; reflex rigidity, 238; in pneumonia, 239
- Abdominal cavity, see peritoneum, 161; sensitivity of its organs, 172; and pain, 172; regulation of blood supply by omentum, 177; infection and omentum, 178; intraabdominal pressure, 181, 200; enteroptosis, 183; hernias, 185; hemorrhage, 233; abscesses, 238; and bacteria, 240; drainage, 244
- Abdominal muscles and abdominal pressure, 183; and defecation, 208; reflex rigidity in peritonitis, 238; rigidity in pneumonia, 239
- Abscess, tropical liver a., 110; multiple a. of liver and thrombophlebitis, 237; in abdominal cavity, 238; perinephritis, 239; abscesses secondary in peritonitis, 245; appendiceal abscess, drainage, 247; secondary pelvic abscesses, drainage, 254; encapsulation of appendiceal abscess, 262; in toxic nephritis, 304; paranephritis, 307; of brain, 414; tuberculous, 466
- Absorption, absorption fever, 166; and temperature, 168; pathological conditions, 168; absorptive power of peritoneum, 170; from bowel, 192; disturbances, 204; ileus, 214; from bowel ileus, 221; intestinal of gas, 225; in ileus, 226; and peritonitis, 243; danger of irrigation with saline solution from increased absorption, 245; delay by camphor oil, 246; difference of indifferent bowel segments, 266; of bladder, 318
- Acapnia, 377
- Acetabulum and pressure on head of femur, 447
- Acetone bodies, 113
- Acholia, 124
- Achylia and diarrhea, 203
- Acid-base equilibrium, 290, 377
- Acidosis, 290, 376
- Acids HCl and Ptyalin, 5; HCl secret. stomach, 41, 69; amino acids, 96, 111; nucleic a., 100, 112, 246; fatty acids in fat necrosis, 103; uric a., 112; bile acids, 124; cholic acid, 130; oleic in bone marrow, 392
- Acromegaly and hypophysis, 327; and club fingers, 482
- Actinomycosis and enteritis, 205
- Addison's disease, 350
- Adhesions about liver, 117; protective, 122; peritoneal, 161; preventatives, 162; of colon, 210; peritoneal, 247, 253
- Adrenal gland shock, 230, 297; and Basedow's disease, 350; and thymus, 352
- Adrenalin, 297; adrenalin symptoms in Basedow, 350
- Agglutinins, spleen, 154
- Air embolism, 398; danger of, 394; death from, 395; brain death, 395
- Air, pressure in chest cavity, 374; residual and complementary, 375; in lungs, 378; in pneumothorax, 379; intra-alveolar, 380; in pleuritis, 385; and changes in respiration, 387; Valsalva's pressure test, 387; in pleural cavity, 390; and divers, 395
- Albumen in spinal fluid, 404
- Albuminuria and tuberc. kidney, 295; orthostatic, 297; lordotic, a., 298; from slight palpation of kidney, 301; permanent after ureteral injury, 303; in constipation, 306
- Alkaloids and liver action, 113
- Alkalosis, 291, 377
- Ammonium salts in blood of portal vein, 112
- Ampula of vater, 126
- Amputation stump and muscle sense, 433

- Amyolytic ferment, 97; of bile, 127  
 Anaphylaxis, 78; and shock, 229, 474;  
     and uremia, 289  
 Anasarca, 465  
 Anastomosis of renal art. and portal vein,  
     117  
 Anemia and gastric ulcer, 77; and spleen  
     preparations, 150; anemia pernicious,  
     129; and splenectomy, 148, 155;  
     myelocytes and myeloid transform.,  
     150; cerebral, 407  
 Anerobic organisms, 240  
 Anesthesia and salivation, 3; and vomit-  
     ing, 46; with chloroform and icterus,  
     114; and thymolymphaticus, 356;  
     and cyanosis, 390; chloroform, a.  
     and embolism, 391; and lung lesions,  
     396; spinal, 404; local anesthesia and  
     inflammation, 459  
 Aneurysm, 478; arteriovenous, 478; aneu-  
     rysmal bruit, 478  
 Ankylosis of a limb, partial, 434  
 Anoxemia, 377  
 Anthrax and duodenal ulcer, 75; and  
     thrombophlebitis, 238  
 Antibodies and spleen, 153; and periton-  
     itis, 239, 246; nucleic acid in gyne-  
     cology, 246; and bone marrow, 463  
 Antipepsin, 70  
 Antiperistalsis, 196, 212  
 Antitrypsin, 99  
 Antrum pylori, 38  
 Anuria and jaundice, 131; reflex a., 283,  
     295; decapsulation, 291  
 Anus, 194-197; sphincter musculature  
     and innervation, 201; Houston's  
     folds, 207; spasms, 207; fissure, 207;  
     prolapsus, 267  
 Aorta, 30  
 Apnea, 375  
 Apoplexy and meteorism, 216; traumatic  
     secondary a. in brain concussion,  
     414  
 Appendicitis, duodenal ulcers, 74; suppura-  
     t. and liver abscess, 135; omentum,  
     179; and cecum, 223, 255; and  
     thrombophlebitis, 238; peritonitis,  
     238; its flora, 240; and blood agglu-  
     tination, 240; early stage, 246;  
     appendiceal abscess drainage, 247;  
     meso-appendicitis, 256; peri-appendi-  
     citis, 256; bacterial flora, 256; ulcers,  
     257; fecal concretions, 258; causes  
     racial and local, 258; perforating a.,  
     260; chronic appendicitis, 262; treat-  
     ment, 263  
 Appendix perforation, 238; and pleura in  
     direct lymphatic communication, 239;  
     gangrene of and putrefactive bac-  
     teria, 240; embolic destruction, 257;  
     valve of Gerlach, 257; position, 258  
 Appetite and gastric stimuli, 80  
 Arachnoidea, changes in epilepsy, 419  
 Arcades, 235  
 Arginase, 190  
 Arteries of stomach, 71, 46; hepatic,  
     110; sup. mesent. 233; coronary  
     injuries, 365  
 Arteriosclerosis, 73; and gastric ulcer, 77;  
     hepatic artery, 117; and cholesterin,  
     132; and embolism, 237; and vene-  
     section, 294; and circulation, 478  
 Arteriovenous aneurysms, 478  
 Arthritic habitus, 454; arthritis de-  
     formans, 445; secondary, 446; and  
     neuropathic bone and joint disease,  
     459; arthritis suppurative, 463; and  
     gonococcus, 464  
 Ascaris in liver, 134; in intestinal spasms,  
     221  
 Ascites and salivation, 6; and stasis  
     portal circulation, 120; and periton-  
     itis, 122; puncture and permanent  
     drainage, 123; peritoneum, 170;  
     polyserositis, 255; and dyspnea,  
     386  
 Asialia idiopathic, 6  
 Asphyxia, 379; from narrowing of respira-  
     tory channels, 389; acute asphyxia,  
     389; and cyanosis, 390; artificial  
     respiration, 390  
 Asthenic constitution, 184  
 Asthma, 388  
 Atelectasis circumscribed, 385, 391  
 Atony of esophagus, 24  
 Atrophy acute yellow, 114; of muscles  
     from rest, 436; of muscles from  
     overstretching, 439; of muscle and  
     bone after nerve section, 441  
 Auto-digestion, gastric, 68; pancreatic,  
     103  
 Auto-intoxication, 224



- Babies nursing, digestion, 42, 190; thymus death, 354
- Bacteremia ileus, 227, 244
- Bacteria and gastric ulcer, 74; and exudate, 121; and spleen, 153; intestinal, 204; in peritonitis, 239; anerobic (toxin formers) 240; infection from contaminated food, 242; peritonitis phagocytosis, 245; predilection for special areas, 257; in toxic nephritis, 304; in blood and tissues, 305; tuberc. in kidneys, 308; in normal lung, 396; and osteomyelitis, 461; and thrombosis, 475
- Bacteriolysins, 463
- Bandages, plaster corset, 52; airtight in pneumothorax, 384.
- Banti's disease, 156
- Banti's disease of infantilism, 157
- Basedow's disease and spleen, 156, 347; War Basedow, 350; and hypophysis, 350; and growth, 351; and islands of Langerhans, 351; and thymus, 353; death, 357
- Bauhins valve, 198-221; cecal distension, 222, 256
- Bile, 58; regurgitation, 58, 113; formation and secretion, 123; bile acids, 124; bile pigments, 124; cholesterin, 124; colorless b., 124; quantity, 124; absence, 124; stimuli, 125; bile acid salts, 125, 127; and digestion, 126; amylolytic enzyme, 127; and peristalsis, 127; stasis, 128; pigments absent; 128; icterus, 130; calculi, 131, ascaris, 134; as culture medium, 134; osteoporosis, 135; concentration, 137; white bile, 138; dilution, 139, bile perionitis, 139; bile pigments, 150
- Bile cylinders, 156
- Bile discharge, 126
- Bile ducts, 123; mucin, 124; disinfection, 124; pressure, 129; ligation, 130; calculi, 133, 134; after cholecystectomy; 136; obstruction, 138
- Bile formation and secretion, 123
- Bile stasis, 128
- Bile thrombi, 129
- Bilharzia, 312
- Biliary calculi, 124-135
- Black and blue marks, hematoidin, 128, 479
- Bladder, urinary innervation, 176, 314; omentum, 179; transplanted intestine, 190; kidneys, 284; extrophy, 285; in hydronephrosis, 301; tuberculosis, 308; calculi, 312; bilharzia, 312; function, 314; innervation, 315; centrum, 315; sensitivity, 316; trabeculated, 317; automatism, 317; absorption, 318; infection, 318; polakisuria, 319; vesical irritation, 319; carcinoma, 319; colds, 319; injuries, 319; regeneration in wounds, 321; sphincter action, 321; prostate, 321
- Bleeders, 73
- Bleeding, parenchymatous, 73
- Blood circulation icterus, 128; shock, 229; interruption by air embolism, 394; obstruction to, 470
- Blood coagulat., 115; destruction of r.b.c. icterus, 128; after splenectomy, 148; destruction of spleen, 150; fluidity in serous cavities, 168; antithrombin, 165; fibrinogen, 165; colloids, crystalloids, 167; agglutination in appendix, 240; blood residual nitrogen, 287; H-ion concentration, 291; increased viscosity in gastric tetany, 361; increased acidity, 376; anemic anoxemia, anoxic anoxemia, 377
- Blood coagulation, liver, 115; delayed in icterus, 130, 162; mesenteric thrombosis, 237; eclampsia, 237; agonal, 473; crystallization center, 473; blood enzymes, 474
- Blood concentration, 286
- Blood distribution respiration, 377, 390; changes of position, 390; in Trendelenburg pos., 390
- Blood pressure depression and ligation port. vein, 119; foramen of Winslow, 120; ileus, 224; fall of in shock, 229; infection, 248; kidney function, 280; in heart lesions, 365
- Blood serum, spleen, 154
- Blood supply, spleen, 154; liver and spleen, 156; regulated in abdomen by omentum, 177; intestinal distension, 223; insufficient and intestinal ulcers, 236; of brain and thyroid, 340; of

- brain, 404-407; of brain and epilepsy, 419; of bone and cartilage, 446
- Blood transfusion, 474
- Blood vessels of peritoneum, 170
- Bloody vomit, 73, 250
- Bone carcinoma and spleen pulp, 150; goiter changes, 352; carotid gland, 364
- Bone fractures, fat emboli, 392; muscle tonus, 428; treatment and functional result, 432; and extension, 432; healing, 435; callous formation, 435
- Bone growth cretinism, 342, 429; repair, 455
- Bone marrow, 129; splenectomy, 149-152; tumors of myelocytes, 150; splenic disease, 157; fat emboli, 392; callous, 435; antibodies, 463
- Bone tuberculosis, 466
- Bones, 427; fracture, 427; muscles and tendons, 428; changes in form, 429; functional adaptation, 429; bone fracture healing, 435; transplantation, 435; pain sensation, 436; atrophy, 430; after nerve section, 441; b. changes and contracture, 444; and cartilage, 446; escaping from joints, 450; bone formation abnormal, 453; overgrowths, 455; osteomyelitis, 460; necrosis, 463; tuberculosis, 466
- Bradycardia, 358
- Brain abscess, 414
- Brain injury and hypophysis cerebri, 328; regulat. of blood supply by thyroid, 340; death from air embolism, 395; brain, 403-426; increase of pressure, 403; function, 403; circulation, 404-407; cerebrospinal fluid, 404; ventricular dilatation, 405; fracture of skull, 407-409; brain pressure and choked disk, 410; dilatation of pupils, 410; concussion, 410; elasticity, 411; contracoup fracture, 412; commotio cerebri, 413; hyperemia, 413; traumatic secondary apoplexies, 414; acute inflammation, 414; encephalitis, 414; prolapsus, 415; meningitis, 415; epilepsy, 415; trephining, 420; operat. surgery, 420; spastic paralysis, 422; literature, 423-426
- Brain pressure, 403-405; choked disk, 410; dilatation of pupils, 410
- Brain tumor, 403
- Branchial clefts, 26
- Breathing CO<sub>2</sub> impoverishment, 229
- Bright's disease, 280, 293
- Bronchial catarrh, 386; enlarged bronchioles and emphysema, 389
- Bruit aneurysmal, 478
- Burns thrombosis, 473
- Bursæ origin trauma, 468
- Buttermilk auto-intoxication, 225
- Cachexia strumipriva, 338
- Calcium balance thymus, 352; parathyroid, 364
- Calculi salivary, 2; biliary obstruction, 128; biliary, 131; urinary and ureters, 302; of kidney, 312; vesical, 312
- Callous healing of fractures, 435; marrow callous, 435
- Camphor oil in peritonitis, 246
- Caput medusæ, 118-122
- Carbon dioxide concentration, 376; impoverishment shock, 229; accumulation and asphyxia, 389
- Carcinoma saliva, 6; of stomach, 60; gall bladder, icterus, 128; spleen pulp, bone carcinoma, 150; rectum and constipation, 207; intestinal, 212; from vesical irritation, 319; of hypophysis, 327; after thyroidec-tomy, 360
- Cardia, 21, 22
- Cardiac failure from bacterial toxins, 248
- Cardiospasm, 23, 68
- Carotid gland, 364
- Cartilage from joints and epiphysis insensible, 436; necrosis, 445; joint mice, 448; cartilage necrosis and osteochondritis, 449
- Casein, 190
- Castration, prostatic hypertrophy, 323; hypophysis cerebri, 325
- Cataract parathyroid tetany, 360
- Catarrh bronchial, 386
- Cathartics and distended bowel, 195, 202; action, 202
- Catheterization, 307; catheter fever, 307
- Cecum, 66; distension, 222; ileocecal junction and adhesions, 254; typhla-

- tony, 264; antiperistalsis, protogenic constipation, 209  
 Cells, ganglion cells of intestines, 193, 221; in anus, 201; in bladder, 314  
 Cerebellum, closure of foramen magnum, 408  
 Cerebrospinal fluid, 404  
 Chaga's disease goiter trypanosome, 346  
 Chest type, 184; tight lacing and enteroptosis, 184; chest cavity, 372-402; gas exchange, 372; pulmonary emphysema, 373; respiratory muscles, 373; diaphragm, 373; tension difference, 374; lungs, 375; respiratory problems, 377; pulmonary vessels, 378; exudates, 379; pleural reflex, 381; enlargement in exudative pleurisy, 385; and pulmonary emphysema, 386; barrel chest, 387; asthma, 388; asphyxia, 390  
 Child birth and trauma, 208  
 Children and the young, appendicitis, 262; anal and rectal prolapse, 268; pyelitis, 304; myxedema, 342; gastric tetany, 360  
 Chloroform poisoning liver, 114  
 Chlorosis and gastric ulcer, 77  
 Cholecystectomy and gastric juice, 41, 52, 135; and pancreatic secretion, 136  
 Cholecystenterostomy, 59, 137  
 Cholecystitis lymphadenitis, 102; calculus, 128; and pain, 139; and thrombophlebitis, 237  
 Cholesterin-calculi, 131  
 Cholesterin-content of bile, 113, 124  
 Cholic acid poisoning, 130  
 Cholin, 338  
 Chondrodystrophy and dwarfism, 328  
 Chorda tympani, 1-5  
 Choroid plexus and spinal fluid, 404  
 Chromaffin system, 341; and status thymolymphaticus, 356  
 Chyle, chyle channels, 113, 126  
 Chyme, 40-55; chyme cleavage, 266  
 Cicatricization of lung cavity, 383  
 Circle vicious, 59; in renal complications, 304; in respiration, 377  
 Circulation stasis of portal, 120; biliary, 125-128; and disturbances in hernia, 219; and peritonitis, 244; pulmonary, 378; capillary and exudates, 379; circulatory disturbances due to increased pressure of r. ventricle, 382; and brain pressure, 403; circulatory disturbances due to weak myocardium, 383; circulation of brain, 404; collateral circulation, 476; circulatory disturbances due to chronic cough, 387  
 Club fingers in chronic chest conditions, 390, 482; peripheral nerve injury, 390; in cardiac lesions, 482  
 Coccyx and anal prolapse, 268  
 Cold and pneumonia, 319; colds and bladder, 319  
 Colitis, 204; pericolitis, 253  
 Collagen and bursæ, 468  
 Colloid chemistry, 11; and gall stones, 131; of bile, 139; in urine, 313  
 Colon secretion, 191; and food, 193; and motility, 193-197; and defecation, 200; fermentation, 203; strictures congenital gonorrheal, 206; and constipation, 209; and adhesions, 210; kinking of splenic flexure, 211; splenic flexure and adhesions, 254; stenosis due to gas blocking, 255  
 Compression of vessels, 390  
 Concussion of brain, 410  
 Connective tissue formation, 253; (adhesions abdominal) in thoracoplasty, 384  
 Consciousness loss of in brain affections, 403; and brain lesions, 409  
 Constipation after gastric operation, 67; and splenectomy, 155; chronic, 206; proctogenic, 206; and rectal carcinoma, 207; constipation muscularis, 208; and hernia, 208; and cecum, 209; spastic, 209; and gastric ulcer, 210; due to pericolitis, 254  
 Constriction of limb and venous stasis, 451  
 Contortionists and omentum, 180; and muscle relaxation, 428  
 Contracture muscular and pain, 176, 444; its influence on bone changes, 444; ischemic, 450; and peripheral nerves, 451  
 Convulsions uremic, 286; in brain affections, 403; in epilepsy, 419  
 Corpora cavernosa and suppuration hematogenous, 461

- Corpus striatum and operations, 421
- Cough and dyspnea, 380; reflex cough from pleura, 381; and circulatory changes, 387; in fat embolism, 393
- Courvoisiers sign, 128
- Coxitis, 443
- Cretinism, 342; and myxedema, 342; and goiter, 343
- Cryoscopy, 282
- Cryptorchism, 329
- Crystalloids, 11; and gall stones, 131; in bile, 139; in urine, 313; in spinal fluid, 404
- Cyanosis, 382; in emphysema, 387; in asphyxia, 390
- Cylindruria, 298; and constipation, 306
- Cystitis, 304; post-operative, 318
- Cystoscopy, 283; in hydronephrosis, 302
- Cysts echinococcus, 111; of hypophysis, 327; cysts and tumors of brain, 421; formation in joints, 468
- Decapsulation of kidney, 291
- Defecation, 197, 200; involuntary, 201; tenesmus, 206; muscles, 208; and spinal cord, 208; and diaphragm, 209; and rectal prolapse, 269
- Deformities from muscular contractures, 445
- Degeneration fibrinoid, 161; yellow of rib cartilages in emphysema, 387
- Deglutition, 13-15
- Diabetes melitus and parotitis, 8; and pancreatic extirpation, 98; and liver metabolism, 111; and cholesterin, 132; diabetes insipidus and hypophyseal extract, 328
- Diaphragm esophagus, 23; hernia, 74; and peritoneal absorption, 167; innervation, 176; and intraabdominal pressure, 182; hernia, 182; and emphysema, 184; defecation, 209; spasm, 215; and singultus, 250; chest cavity, 373; paralysis, 373-386; movements, 374; low position, 382; in pleuritis, 385; and dyspnea, 385; and emphysema, 386
- Diarrhea and gastroenterostomy, 60; and lactose, 191, 202; pathological, 202; egg albumen, 204; and ulcers, 205; and pneumococcus peritonitis, 244; after bowel resection, 265
- Diastatic enzymes of intestines, 191
- Digestion and saliva, 4; and bile, 126; intestinal and bile in stomach, 138; and spleen, 154; bowel digestion, 192; and diarrhea, 203; of fat, 266
- Disc choked in brain affections, 403, 410; in war wounds, 410
- Divers air embolism, 395
- Diverticuli of esophagus, 25; congenital, 26; Meckel's, 257
- Douglas' cul de sac, 53; and bowel rupture, 232; pus collection in, 257; drainage, 253; in rectal prolapse, 261; in children, 268
- Drainage, 251; 253
- Ducts of Stenson, 10; Wharton's, 10; their ligation, 13; of pancreas, 95, 102; thoracic, 98; ligation, 244; common d., 102; Thoracic and bile, 128
- Duodenum, duodenal cap, 40; ulcers, 40, 68; fistula, 40; duodenal back flow, 59; ulcers, 74; from appendicitis, from tonsillitis, 75; tubercle bac., 75; hunger pain, 78; and bile flow, 126; stasis, 137
- Dysentery, tropical, 135
- Dyspepsia, fermentation, 203; intestinal, 204-224; and appendicitis, 263
- Dysphagia of valsalva, 18
- Dyspnea lusoria, 30; fermentation dysp., 203; thymus complication, 354; and cough, 380; dyspnea and pneumothorax, 381; and diaphragmatic paralysis, 386; and emphysema, 386; inspiratory, 389; and goiter, 389
- Dysthyreosis, 348
- Dystrophy adipose genital, 327
- Echinococcus cyst, 111
- Eck's fistula and pancreat. necrosis, 105; liver activity, 110-111; and urine, 112; chloroform, 113; liver eliminat., 119
- Eclampsia and blood coagulation, 237; convulsions, 286; edema of brain, 288; hypertension theory, 288; fat emboli, 392
- Edema of bowel, 217; and thyreopriva, 340; edema of brain and eclampsia,



- 288; tendency to, 289; of neck and Stock's collar, 358; and venous stasis, 451; edema of nephritis, 451; of syringomyelia, 481
- Effusions and tension, 443
- Elbow luxation, 454
- Elephantiasis Arabian and Graecorum, 481
- Embolism gastric ulcers, 72; bacterial, 74; and thrombosis differentiated, 237; pulmonary fr. appendicitis, 260; pulmonary emboli, its operation, 390; retrograde, 391; fat emboli, 392; their course, 392; paradox embolism, 392; air embolism, 394; cerebral, 407
- Emphysema diaphragm, 184; pulmonary, 386; and heart, 386; Valsalva's pressure test, 387; cyanosis, 387; and rib, 387; vicarious, 388; marginal emphysema, 389; occupation factors, 389; from narrowed respiratory channels, 389
- Empyema of gall bladder, 186; opened empyema and air embolism, 395
- Encephalitis, 414
- Endocarditis and emboli, 392; murmurs, 478
- Endotoxins in acute osteomyelitis, 462
- Enema and margin current, 194
- Enteritis, 204; and poisons, 204; acute enteritis, 205; renal, 205; and bacterial infect. of peritoneum, 242
- Enterokinase, 96, 104, 190
- Enteroptosis and abdominal pressure, 183; origin, 184; filling of arm, 184; chest cavity, 373
- Enterostomy, 225
- Enzymes gastric, 42-69; pancreatic, 96; of liver, 110; uricolytic ferments, 112; inhibition, 115; amylolytic of bile, 127; tryptic enzyme in bile, peritonitis, 139; adhesions, 162; leucocytes as enzyme carriers, 162; intestinal, 190; enterokinase, 190; erepsin, 190; arginase, 190; nuclease, 190; lactase, 191; in suppurative peritonitis, 243
- Epididymitis, tuberc., 311-320
- Epigastrium blunt trauma, 230
- Epiglottis, 16-20
- Epilepsy and edema of brain, 288; tetany, 363, 415; true and traumatic, 416; and poisoning, 418; from bacterial toxins, 418; syphilis, 418; following puncture of ventricle, 420
- Epiphyseal osteomyelitis, 461
- Epiphyses changes after thymectomy, 352
- Epityphlitis, 255
- Erepsin, 190
- Ergot-poisoning tetany, 361
- Erosions gastric, 38, 73; uremic, 79
- Esmarck bandage and spina bifida, 460; and hyperemia, 477
- Esophagus carc. and salivation, 2-13; innervation, 19-44; deglutition, 21; narrowing, 22; sphincter, 22; and cardiospasm, 23; paralysis, 24; atony, 25; diverticula, 25; disturbances, 27; organic stenosis, 27; perforation, 28; scarlet fever, 28; ulcers, 28; esophagomalacia, 29; rupture, 29; esophagotomy, 30; dysphagia, 30; esophageal stenosis and gastrostomy, 80; literature of saliv. glands and esoph., 30-35; esophageal varices fr. cirrhosis of liver, 122
- Ether, 2, 3; and saliva, 2; in peritonitis, 473
- Eunuch, 325; and geroderma, 327
- Exhaustion and nerve shock, 229
- Exner's needle reflex and intestinal contractions, 194
- Exophthalmic goiter, 347; nervous signs, 349; and adrenalin, 350; differentiation, 353
- Exostosis and esophag. ulcers, 28
- Extension and bone fracture, 432
- Extremities, 427-492
- Exrophy of bladder, 285; and pain, 316
- Exudates, transudates, ascites, 121; and chest cavity, 379; in pleuritis, 385
- Eyes from ectodermic cells, 457
- Fasting and nitrogen loss, 114
- Fat absorption, 113, 126, 266; in vessels saponified, 393
- Fat embolism, 126, 392; in eclampsia, 392; in greater and in lesser circulation, 393
- Fat necrosis, 102

- Fat synthesis, 193  
 Fatigue and partial paralysis, 434  
 Fecal fistula and skin irritation, 191;  
     action of fistula, 221; and tamponade,  
     251  
 Fecal impaction, 219  
 Fecal obstruction, 209  
 Fecal retention incarcerat., 217; fecal  
     stasis, 210; ileus, 212-219; fecal  
     toxicity, 225  
 Fecal vomiting, 212  
 Feces acholic, 124-128; decomposition,  
     126; bile stained with icterus, 128;  
     composition, 191; starvation, 192;  
     quantity, 192; involuntary evacua-  
     tion, 201  
 Fermentation dyspepsia, 203  
 Ferments, lab ferment, 41; uricolytic, 112;  
     of thymus, 353; tryptic of poly-  
     morph leucos., 466; in synovial  
     fluid, 468  
 Fibrinogen, 115, 165  
 Fibrinuria, 314  
 Filaria, Bancroft's and Arabian ele-  
     phantiasis, 481  
 Fingers, club fingers, 390, 482; webbed  
     fingers, 416; polydactylism, 416  
 Fissure in ano, 207; and intest. spasms,  
     222  
 Fistula salivary, 1-13; from neck to  
     stomach, 21; pancreatic, 96; gall blad-  
     der, 101, 124, 135; Eck's, see there,  
     intestinal, 190; discharge, 203; intes-  
     tinal in surgery, 221; tuberculous  
     and difficult healing, 466  
 Flat foot leading to atrophy of leg mus-  
     cles, 439; contractures, 443  
 Food defective evacuation, 51; and bowel  
     absorption, 193  
 Foramen of Winslow and blood pressure,  
     120; foramen ovale and emboli, 392;  
     f. of Magendi's, 405; foramen mag-  
     num, 408  
 Foreign bodies, see calculi, in fracture of  
     skull, 411  
 Fracture of skull, 407-409; and foreign  
     bodies, 411; of bones, 427; of patella,  
     431; treatment and functional result,  
     432; of bone and rest position, 432;  
     of metastarsals, 444  
 Furunculosis, 304  
 Gall bladder, galactose, 111; and liver, 110;  
     cholecystenterostomy, 59, 137; and  
     chr. pancreatitis, 101; and lymphad-  
     entitis, 102; and bile, 123; cho-  
     lesterin, 124; movements and its  
     innervation, 126; and icterus, 128;  
     shrunk, 128; and pancreatic tum-  
     ors, 128; Courvoisier's sign, 128;  
     hydrops., 129, 133, 138; gall stones,  
     124, 131; and surgery, 135; chole-  
     cystectomy, 135; function of, 185;  
     Oddi's sphincter, 102, 105, 136;  
     enlargement of stump after removal,  
     136; and bile concentration, 137; bile  
     peritonitis, 139; rupture, 140, 240;  
     literature of liver and gall bladder,  
     141-147; gall bladder operations  
     and omentum, 180; cholelithiasis  
     and meteorism, 215; and peritonitis;  
     240  
 Gall stones, 124-131; gall stone colic, 133;  
     and diet, 134; and surgery, 135  
 Ganglion, Jackson's, 5; Gasserian, 14; of  
     cardia, 24; intragastric, 41  
 Gangrene and ileus, 215; and hernia, 219;  
     and retrograde incarceration, 220;  
     after bowel injury, 233; from cold,  
     473  
 Gas exchange, absence in pneumothorax,  
     358, 372; decrease and resection of  
     spinal cord, 422  
 Gastric crises, 49  
 Gastric diseases, 49ff  
 Gastric juice, 41, 47, 61; and splenectomy,  
     154  
 Gastric mucus and antienzyme, 62  
 Gastric resection, 64ff  
 Gastric secretion, 39  
 Gastric ulcer pain irr., 47; and trypsin,  
     59, 61, 68, 71; and arteriosclerosis, 77;  
     and chlorosis, 77; reflex ischemia, 79;  
     and constipation, 209  
 Gastric wounds, 63  
 Gastrin, 42, 96  
 Gastritis, 48  
 Gastroduodenostomy, 56  
 Gastroenterostomy, 54, 55; and diarrhea,  
     60; and healing of gastric ulcer, 79  
 Gastrointestinal inflammation and throm-  
     bophlebitis; 238  
 Gastrointestinal innervation, 44

- Gastroptosis of Glenard, 53, 79  
 Gastrostomy, 80  
 Genitalia female and peritonitis, 240;  
   pneumococcus peritonitis, 242; and  
   cystitis, 318; and thyreopriva, 340;  
   generative glands and thymus, 352  
 Genu valgum, 447  
 Geroderma, 326  
 Giantism and hypophysis, 327, 482  
 Glands, endocrine and exophthalmus, 350;  
   and thymus, 352  
 Glands, salivary, 1; salivary and sexual  
   glands, 7; literature, 30; digestive,  
   39; Brunners, 58; emptying action,  
   125; lymph glands and splenectomy,  
   149; parotid gland, 257; pineal, 326;  
   hypophysis cerebri, 326; endocrine  
   glands in exophthalmus, 350  
 Glaucoma of kidney, 292  
 Glottis and inspiration, 182, 187  
 Glycogen, 111; decrease, 130  
 Glycosuria, 98; in exophthalmus, 350  
 Goiter, 20, 338; and cretinism, 343;  
   cause, 343; distribution, 344; due to  
   a Brazilian trypanosome, 346; ex-  
   ophthalmic, 347; and thymus, 353;  
   death, 357; and respiratory diffi-  
   culty, 389  
 Gonorrhea strictures of colon, 206; and  
   occlusion of efferent ducts, 330; and  
   suppurative arthritis, 464  
 Gout, renal and true, 112; urine in gout,  
   313; and arthritis deformans, 448  
 Grafe's sign, 349  
 Harelip, 18  
 Head lesions, 407, 409, 414, 420  
 Healing of aseptic operative incisions, 454  
 Heart, 364-366; heart failure, 224;  
   cardiac disease and embolism, 237;  
   surgery, 364; bundle of Hiss, 365;  
   pericardial hemorrhage, 365; in-  
   juries to coronary arteries, 365; peri-  
   carditis, 366; blunt force, 366; dilat.  
   r. ventricle and dyspnea, 380; pleura  
   reflex, 380; heart condition and  
   cyanosis, 382; myocardial weakness  
   and circulatory disturbance, 383;  
   and emphysema, 386; heart action  
   in acute asphyxia, 389; and air  
   embolism, 394; heart sounds, 479  
 Hematemesis and gastric ulcer, 72; and  
   peritonitis, 250  
 Hematoidin, 128  
 Hematoma, icterus, 129  
 Hemoglobin iron free, 129; regenerat. after  
   splenectomy, 148  
 Hemolymph nodes, 151  
 Hemolysins in osteomyelitis, 463  
 Hemolytic diseases, 157  
 Hemorrhage in serous cavities, 163; mas-  
   sive in kidney bed, 298; and brain  
   concussion, 414  
 Hemothorax, 163  
 Hepatitis, see liver  
 Hepato-cholangio-enterostomy, 138  
 Hernia and omentum, 181; diaphragma-  
   tic, 182; development, 185; umbilical,  
   186; and constipation, 208; meteor-  
   ism, 216; incarcerated, 218; rupture,  
   232; reduction of, leading to trauma  
   of intestines, 233; strangulation, 237;  
   and peritonitis, 241; sliding hernia,  
   269; perineal hernia, 269; scrotal,  
   329  
 Hirschsprung's disease, 207  
 Hormones gastric, 41; pancreatic, 98; and  
   splenectomy, 152-155; and renal  
   stimuli, 282  
 Houston's folds, 207  
 Hunger mechanism, 48; and gastric  
   operat., 66, 78  
 Hydrocephalus, 403; and spinal fluid, 405  
 Hydrogen ion concentration saliva, 2; in  
   renal conditions, 290; of blood, 376  
 Hydronephrosis cause of death, 287, 291,  
   300  
 Hydrops of gall bladder etc., 129-138  
 Hydrothorax and salivation, 6  
 Hygroma, 468  
 Hyoid bone, 16, 18  
 Hyperemia of relaxation, 183, 234  
 Hyperesthesia and brain lesions, 175  
 Hyperglycemia, 98  
 Hypernephroma, 297  
 Hyperpnea, 377  
 Hyperthyroidism, 346  
 Hypophysis cerebri castration, 325; physi-  
   ology, 326; action, 327; acrome-  
   galy, 327; menopause, 327; adipose  
   genital dystrophy, 327; tumors, of  
   327; obesity, 327; extracts in treat-

- ment, 228; enlargement after total thyroidectomy, 341; Basedow, 350
- Hypospadias hydronephrosis, 301
- Icterus galactose, 111; following chloroform anesthesia, 114; bile flow, 128; obstruction, 128; hemolytic or toxicemic icterus, 128; Kupfer's star cells, 129; catarrhal, familial, neonat., 129; hematoma, 129; results of icterus, 130; delayed coagul. of blood, 130; subarachnoid fluid, 405
- Ileocecal junction and adhesions, 254
- Ileocolic muscle, 198
- Ileum, 42, 45, 61, 191; invagination, 199; weakness, 203; resection, 265
- Ileus arteriomesenteric, 51; abdominal pressure, 183; rectal carcinoma, 207; chr. intestinal intoxicat., 212; pain, 212; dynamic, obturation ileus, 212; paralysis of bowel, 214; retrograde incarceration, 220; invagination, 220; paralytic ileus, 221; spastic, 221; due to lead, 221; ascaris ileus, 222; distension, 223; auto-intoxication, 225; enterostomy, 226; bacteremia, 227; acute pancreatitis, 228; intestinal noises, 228; and peritonitis, 249; necrosis of kidney, 306
- Iliac fossa and intestinal trauma, 230
- Immunization, 246
- Inactivity muscular atrophy, 436
- Incarceration elastic, 216; fecal, 217; relaxed inc., 219; retrograde, 220-237; renal, 300
- Infarcts red. liver, 118; hemorrhagic, 234; anemic infarction, 234
- Infection omentum, 178; direct hematogenous, 257; of kidneys, 305; tetany, 361
- Innervation of salivary glands, 1; of tongue, 13; esophagus, 19; stomach, 41; pancreas, 95; of hepat. vessels, 125; gall bladder movements, 126; intestinal bacteria, 176; bladder, 176, 314; diaphragm, 176; intestines, 198; of distal end of intestines, 201; anus, 201; crossed, 315
- Intestinal absorption of food, 193
- Intestinal catarrh, 203
- Intestinal contents toxicity, 225
- Intestinal fistula, 190
- Intestinal gases, 213
- Intestinal infarct, 234
- Intestinal juices regurgitation, 59, 190; secretion, 191
- Intestinal tract innervation, 176
- Intestinal ulcers, 61
- Intestinal wall, 55
- Intestines, law of, 44; strength, 45; operation sutures, 55; intestinal juice regurgitation, 59, 172; intestinal mucosa, 62; bile, 123; fecal decomposition, 126; jaundice, 128; sensitivity operations, omentum, 180; enteroptosis, 184, 190; length, 190; transplantation, 190; secretions, 190; enzymes, 190; lactase, diarrhea, 191; secretory stimuli, 191; paralytic secretion, 191; pancreas, 191; hormonal stimuli, 191; feces, 191; sensitive bowel, 192; absorption, 192; food, 193; intest. movements, 193; mixing movements, 193; marginal current, 194; peristaltic wave, 195; cathartics, 195; rolling movement, 195; anti-peristalsis, 196; motion, its nerve supply, 198; sphincters, 198; invagination, 199; defecation, 200; anal innervation, 202; diarrhea, 202; bowel weakness, 203; enteritis, 204; poisoning, 204; chronic inflammation, 205; ulcer, 205; tenesmus, 206; chronic constipation, 206; rectal carcinoma, 207; anal fissure, 207; covered sensitivity, 208; constipation surg. of colon, 211; intestinal intoxication, 212; ileus, 212; paralysis of bowel, 214, 249; meteorism, 215; trauma, 216; incarceration, 216; edema, 217; hernia, 218; paralyt. ileus, 221; evacuation before surgery, 221; lead colic, 221; ascaris ileus, 222; tabetic crises, 222; stercoral ulcers, 223, 231; auto-intoxication, 225; ileus intestinal noises, 228; manipulation of, 1; shock, 228; blunt trauma, 230; rupture, 231; injury from reducing a hernia, 233; gangrene of, 235; ulcers, 236; stenosis, 236; peritonitis, 238; chr. peritonitis, 250; resection, 263; chyme cleavage, 266; fat digestion, 266; literature, 269-278; permea-



- bility of walls to bacteria, 286; renal disease, 305
- Intestines, large, secretion, 191; sigmoid flexure, 193; movements, 197; defecation, 197; constipat., 206; surgery, 211; vascular supply, 236; pericolicitis, 253; typhlatony, 264; rectal prolapse, 267; sliding hernia, 269; perineal hernia, 269
- Intoxication intestinal, 225
- Intraabdominal pressure, 181; and defecation, 200
- Intussusception, 198-220
- Invagination of bowel ileocecal, 198-220
- Iodine Basedow, 347
- Iodothyreoglobulin, 338, 363
- Iodothylin, 338, 348
- Iron content of food, blood regeneration 148
- Iron metabolism splenectomy, 149, 152; Banti's disease, 157
- Ischemic contracture, 450
- Jaundice obstr. galactose, 111, 128; toxic, 130; anuria, 131; spleen, 156
- Jejunum, 53; prosecretin, 57; ulcers, 62-68; food, 193; tearing of, 232; resection, 265
- Joint capsule muscle tonus, 428; joint cartilage insensibility, 436; shrinkage, 442; joint mice and arthritis deformans, 450; to prevent refilling and shrinking, 466
- Joints, 427; muscle tonus, 428; muscle, equilibrium, 432; joint mice, 436, 448; joint disease, 438; stiffening and contracture, 441; air mobilization, 442; rheumatism, 442; arthritis deformans, 445; joint movements, 447; osteochondritis dissecans, 449; infection in suppurat. arthritis, 464; destruction of, 465; artificial mobilization, 467; formation of 467; synovia, 468; resection, 469; transplantation, 469
- Keloid formation, 453
- Kidney hyperglycemia, 98; and peritoneal absorption, 167; renal calculi meteorism, 215; gunshot wounds, perinephritic abscess mistaken for peritonitis, 239; inflamm., 257; bladder, male genitalia, hypophysis, 279-337; unilateral renal disease, 279; threshold, 279; microscopic function, 279; reabsorption, 280; functional tests, 280; Bright's disease, 280-293; nephritis, 281; polyuria, 281; nerve supply, 282; salt puncture, 282; hormones, 282; pain, 283; reflex anuria, 283; cystoscopy, 283; normal secretion, 283; polyuria, 284; pollacissuria, 284; tubercul. nephritis, 284; retention, 285; uremia, 286; concentration, 286; kidney wasting, 287; parabiologic tests, 287; eclampsia, 287; acid base equilibrium, 290; acidosis, 290; H-ion concentration, 290; alkalosis, 291; decapsulation, 291; renal insufficiency, 291; uranium, sublimite poisoning, 292; glaucoma of kidney, 292; transplantation, 293; relations between the two kidneys, 294; blunt injury, 295; healing of wounds, 295; and adrenals, 297; massive hemorrhage in kidney bed, 298; floating kidney, 298; fixation of kidney, 299; Dietl's crises, 300; torsion, 300; pelvis, pain, 300; hydronephrosis, 301; dilatation of pelvis, 303; pyonephrosis, 304; toxic nephritis, 304; infections, colon bacilli, 305; relat. of kidney to bowel, 305; necrosis of kidney, ileus, 306; paranephritic abscess, 307; tuberculosis, 308; calculi, 312; literature for kidney, bladder, male genit. hypophysis, 330-337
- Knee joint contracture, 444
- Kupfer's star cells, 129, 151
- Kyphosis respiration, 388
- Lacing, enteroptosis, 184; renal ptosis, 299
- Lactase diarrhea, 191
- Langerhan's islands and diabetes, 99; Basedow's disease, 351
- Laparotomy scars, bone formation, 453
- Larynx, 16
- Lead colic, 207, 221
- Lecithin fat synthesis, 193
- Leg ulcers varicose veins, 475; nervous origin, 476; nerve stretching, 476

- Leg wounds difficult healing, 470; lepra, elephantiasis graecorum, 481
- Leukocytosis phagocytosis in peritonitis, 245; in appendicitis, 260; in spinal fluid, 404; phagocytosis in suppurative arthritis, 465; lymphatic in tuberculosis, 466
- Leukourobilin, 124
- Ligamenta varioforma, 210
- Ligamentum hepato duodenal venous dilat., 118; hemorrh. of liver, 120; phrenico-colic, 254
- Ligation of hepatic art., 117; portal vein, 118
- Lipase, 41, 97
- Liver, 110; thrombosis in after ligation of omentum, 72; physiology, 110; tropical abscess, 110, 135; cirrhosis, 110; independence of lobes, 110; regenerative power, 110; echinococcus cysts, 111; carbohydrate metabolism, 111; glycogen, 111; galactose, 111; purin, nucleoprotein metabolism, 112; uricolytic ferments, 112; fat absorption, 113; acetone bodies, 113; detoxifying property, 113; phosphorus poisoning, 113; chloroform poisoning, central necroses, 113; trypsin, 114; acute yellow atrophy, 114; protein sparing, 115; repair, 115; blood coagulation, 115; antithrombin, 115; surgery, 115; ligat. and anastomoses of vessel, 111; red infarcts, 118; caput medusæ, 118, 122; closure portal vein, 118; Eck fistula, 119; obstruct. hep. vein, 119; checking of hemorrhage, 119; ascites, stasis port. circul., 120, 170; cirrhosis, 121; splenic tumor, 121; Talma's operat., 122; esoph. varices, 122; permanent drainage, 123; bile formation, secretion, 123; bile acids, 124; cholesterin, 124; acholic stools, 124; white bile, 124; curve of secret., 125; biliary circulation, 125; icterus, 128; Kuffer's star cells, 129, 151; hepatic insufficiency, 130; hematogenous infection, 135; suppur. appendicitis, 135; injuries, 140; literature, 141-147; liver and spleen, 150-152; bile cylinders, 156; omentum, 178; thrombophlebitis, 237; Pick's pseudo-cirrhosis, 255; Zuckergussleber, 255
- Local anesthesia and inflammation, 459
- Lordosis, 53, 298
- Lumbar anesthesia, 404
- Lumbar puncture uremia, 288
- Lung paranephritic abscess, 307; oscillation, 358; expansion, wounds in heart, 365; elasticity, 373; collapsed l., 375, 384; lung activity, body position, 375; respiratory movements, 375; respiratory center, 375; respiratory innervation, 375; CO<sub>2</sub> content of venous blood as respiratory stimulant, 375; apnea, 376; H-ion concentration, 376; pulmonary circulation, 378; pneumothorax, 379; intralveolar pressure, 380; pneumothorax, 381; dyspnea, 381; pendulum air, 382; cyanoses, 382; increased, decreased pressure, 383; pleuritis, 383; closed pneumothorax, 383; thoracoplasty, 383; paradox respiration, 380; obliteration of cavity in pneumothorax, 384; redistension of hilus, 385; exudative pleuritis, 385; atelectasis, 385; diaphragmatic paralysis, 386; pulmonary emphysema, 386; bronchitis, 386; emphysema, 387; changes in thoracic cavity, kyphosis etc., 388; enlargement due to dynamic causes, 388; asphyxia, 389; artificial respiration, 390; pulmonary emboli, 390; air emboli, 393; post-operative lung complications, pneumonia, 395; from anesthesia, 396; bacteria in l., 396; war gases, 396; hemorrhages, 397; edema, 397; trauma, 398; literature, 398-402
- Luxation of elbow, 454
- Lymph, colloids, 167
- Lymph glands, spleen, 149-152; of omentum, 178; mesenteric bacilli, 305; enlargements and status thymolympathicus, 355
- Lymph vessels of omentum, 179; collapsed lung, 384; of lung, 396; flow of lymph, 480; regeneration, 480; tuberculosis, syphilis, 481
- Lymphadenitis, 102
- Lymphangitis, 102

- Lymphatic diseases, stasis, elephantiasis, 481
- Lymphatic edema, 481
- Mediastinal palpitation, 358
- Mediastinum compression, 357; emphysema, 358; tumors, 358; lymph channels, 358; kinking, 382; oscillations, 383; after pneumothorax, 385; in pleuritis, 385
- Medulla oblongata deglutition center, 20; vomiting center, 45; paralysis of vaso-motor center by bacterial toxins, 248; respiratory center, 375; increased pressure, 403, 409; brain concussion, 443; in epilepsy, 417
- Meningitis sacculated, 404, 415; meningitis serosa, 415
- Menopause hypophysis, 327
- Mercury poisoning enteritis, 204; renal activity, 292
- Mesenteric veins kinking, 219
- Mesenteric vessels kinking, 219; injury from pressure, 233; aneurysm, 237
- Mesentery, 233; tears, 236
- Mesocolon ligat. of veins in thrombophlebitis, 238
- Metabolism of carbohydrates, 98; fat, 99; protein, 100; and liver, 110; cellular, ascites, 121; cholecystectomy, 136; iron metabolism, 149, 152, 157; spleen, 154; disturbances from resection of bowel, 265; thyroid, 340; thymus gland, 351; calcium metabolism, 352, 448
- Metastasis, tumor spleen, 154
- Meteorism splenectomy, 155; ileus, 212; differentiation, 213; diaphragm, 215; nerve involvement, 215; abdominal tumors, 215; renal and biliary calculi, 215; hysteria, 216; tabes, 216; in apoplexy, 216; after blunt trauma, 216; localized Bauhin's valve, 222; solar plexus, 249
- Milk digestibility for adults, 191
- Momburg's belt compression of vessels, 391
- Momburg's tube, 233
- Mouth hygiene, 4; wounds, 4
- Murmurs of endocarditis, 478; venous murmur, 479; arterial, 479
- Murphy button, 55, 63
- Muscles of tongue, 15; orbicularis, 18; of deglutition, 19; of defecation, 208; 427; fracture of bones, 428; tension, 428; muscle tonus, 428; contortionists, 428; muscle anlagen, 429; form of muscle and skeleton, 429; development, 429; muscle fibers, 430; muscles of spine of sea urchin, 430; threshold of muscle tension, 430; nerves in muscle, 430; peripheral stimuli, 430; injury, 430; atrophy, 431; deformity, 431; muscle equilibrium, 432; paralysis, 432; muscle sense, 432; deep sensations, 433; muscle transplantation, 434; learning a new function, 434; regeneration, 435; size and strength, 437; endurance muscle, 437; atrophy from overwork, 437; internal and external work, 438; joint disease, 438; kinetic chains, 440; atrophy after nerve section, 441; ischemic contracture, 451; venous stasis, torticollis 452; myositis ossificans, 453; traumatic, 454; neurotisation, 456
- Myasthenia, parathyroid, 362
- Myelocytes spleen, 150
- Myositis, ossificans, 453; traumatic, 454
- Myotonia and parathyroids, 362
- Myxedema, 338, 340; in adults, 341; cretinism, 342
- Necrosis, focal after omental thrombosis, 72; pancreatic, 102; central of liver, 113
- Nephrectomy, 294
- Nephritis, 9; enteritis, 205, 284; tuberculous, 284; eclampsia, 286; acute and eyeground, 288; decapsulation, 292; from floating kidney, 301; toxic, 304; suppurative, 304; edema, 451
- Nephrolysins, 287
- Nerve degeneration, 456
- Nerve disease bone overgrowths, 455
- Nerve injury peripheral and club fingers, 390; brain pressure, 403; healing, 456; pain, 458
- Nerve resection muscular atrophy, 441; neuroma, 456

- Nerve severance, 456  
 Nerve stretching of motor nerves, 457;  
   neuralgia, 458; neurolysis, 459; neuro-  
   kynese, 459; and freezing of nerve, 458  
 Nerves of salivary glands, 1; of tongue, 13;  
   of esophagus, 19; stomach, 41; pan-  
   creas, 94; hepatic vessels, 125; gall  
   bladder, 126; of peritoneum, 171;  
   intestinal tract, 176; bladder, 176;  
   diaphragm, 176; splanchnic in gastr.  
   innervation, 44; vagus in gastr.  
   innervation, 44; sympathetic, 44;  
   pain, 174; constipation, 209; in  
   respiration, 376; nutritive stimulus,  
   376; muscle tonus, 430; paralysis,  
   432; transplantation, 452, 457; anas-  
   tomosis, 457; trophic and muscular  
   atrophy, 459  
 Neuralgia, 458  
 Neurasthenia and auto-intoxication and  
   sphincter tonus, 207  
 Neuritis, 458  
 Neuroma, 456; prevention of, 456  
 Neuropathic arthritis, 459  
 Neurotization, 456  
 Nitrogen renal elimination, 285; residual,  
   286  
 Nuclease, 97, 190  
 Obesity, hypophysis cerebri, 327  
 Obstruction of flow of bile, 128; see also  
   under ileus.  
 Occupation tetany, 361  
 Omentum resection and gastric ulcer, 72;  
   resection and vomiting, 148; ab-  
   sorption, 168; gastr. ulcer pain, 174;  
   greater function, 176; liver necroses,  
   177; regulator of abdom. blood  
   supply, 177; protective function, 177;  
   lymph nodules, 178; foreign bodies,  
   178; wounds, 179; gall bladder  
   operations, 180; its removal, 181;  
   torsion, 181; strangulation, 215;  
   in decapsulation of kidney, 292  
 Oral cavity, 1  
 Orchitis tuberculous, 312  
 Osmosis of intestinal wall, 192; renal  
   activity, 288  
 Ossification cretinism, 340; thymus endo-  
   chondral, 352; osteoarthropathy of  
   Pierre Marie, 482  
 Osteochondritis dissicans, 449  
 Osteomalacia parathyroids, 362; muscle  
   contracture, 445  
 Osteomyelitis, 460; infection, 461; causes,  
   463; hemolysins, 463  
 Osteoporosis, absence of bile, 124, 135  
 Ovariectomy and parotitis, 9  
 Oxamid calculi, 314  
 Oxygen, 376; respiration, 376  
 Pacchionian bodies and spinal fluid, 405  
 Pacinian corpuscles, 4; pleura, 380  
 Pain in gastric ulcer, 47, 174; in chole-  
   lithiasis, 139; in subcutaneous hemor-  
   rhage, 166; intestines, 173; in ulcera-  
   tive processes, 174; muscul. con-  
   traction, 175; enteroptosis, 185; in  
   anus, 207; abdominal and ileus, 212;  
   appendicitis, 223; anesthesia, 229;  
   in peritonitis appendiceal, 260; in  
   renal affections, 283; in renal ptosis,  
   300; in urethra, 315; pleura, 380;  
   muscle sense, 432; bone, 436; nerve  
   injury, 458  
 Palate and taste, 14; cleft, 18  
 Palpation slight of kidney and albuminu-  
   ria, 301  
 Pancreas, 95; enzymes, 57; secretion and  
   secretin, 57, 96; function, 95; ducts,  
   95; innervation, 95; secretin and  
   gastrin, 96; stimuli, 96; juice, 96;  
   fistula, 96; lipase, 97; trypsin, 97,  
   amylase, 97; nuclease, 97; steapsin;  
   102; extirpation, 98; diabetes, 98;  
   pancr. hormone, 98; islands of  
   Langerhans, 99; ligation of ducts, 99;  
   internal secretion, 100; chronic pan-  
   creatitis, 101; lymphangitis, 102;  
   bile, 102; pancr. necrosis, 102-105;  
   intravital self digestion, 103; entero-  
   kinase, 96, 104; sphincter of Oddi,  
   102-105; literature, 106-109; bile,  
   127; pancreat. secretion and cho-  
   lecystectomy, 136; and intestinal  
   secretion, 191; acute and ileus, 228;  
   superior mesent. vein, 235; islands of  
   Langerhans in Basedow's disease, 351  
 Papilla of Vater, 57; innervation, 126;  
   Oddi's sphincter, 102, 105, 136, 140  
 Paracentesis for exudative pleuritis, 385  
 Paradox embolism, 392



- Paradox respiration, 359, 383
- Paralysis of tongue, 17; of esophagus, 24; ileus, 51; bulbar p., 20; in strangulation ileus, 214; reflex p., 216; of bowel in hernia, 219; intestinal and peritonitis, 249; diaphragm, 386; respiratory, brain affection, 403; spastic, 422; infantile p., nerve transplantation, 457; of a limb and pain, 458
- Paraplegia, 421
- Parasites, echinococcus cysts in liver, 111; ascaris in liver, 134; ascaris ileus, 222
- Parathyroids, 341, 359; tetany, 359; Chvostek's phenomenon, 359; accessory p., 360; trophic disturbances, 360; latent tetany, 360; epilepsy, 362; myotonia, 362; myasthenia, 362; detoxifying action, 363; transplantation, 363; calcium metabolism, 364
- Parotid gland, 1; inflammat., 257
- Parotitis, 8; saliva, 7; and diabetes, 8; post-operative suppurative, 8; orchitis, 9; ovariectomy, 9; Stenson's duct, 10; Wharton's duct, 10
- Passavant's cushion, 16
- Patella fracture, 431
- Pellagra veins, 472
- Pelvis renal, 303; infection, 304; tuberc., 309
- Pendulum, air, 382
- Pepsin, 52, 57; after splenectomy, 154
- Peptids, splitting of food, 192
- Perforation peritonitis, 240; of stomach difference whether by ulcer or carcinoma, 241
- Pericarditis, 365
- Pericardium, 162; hemorrhage, 365
- Pericolitis, 253; pneumonia, 254; cause of constipation, 254
- Perihepatitis, 255
- Perinephritic abscess, 239
- Periosteum bone transplantation, 435; pain, 436; myositis ossificans, 454
- Periostitis, occupational, 454
- Peristalsis of esophagus, 21; gastric, 37; stimul. by bile, 127; absorption, 169; reverse p., 45; omentum, 176; abdominal pressure, 182; hernial loops, 216; of ureters, 302; in vas deferens, 311
- Peritoneal shock, 166; resistance, 185
- Peritoneum infection, gastr. ulcer, 72, 161; embryology, 161; anatomy, 161; function, 161; adhesions, 161; encapsulation of foreign bodies, 162; similarities of diff. serosa, 163; hemorrhage, 163; shock, 166; total surface, 166; process of absorption and exudation, 166, 178; and urine, 167; colloids and crystalloids, 167; diaphragm, absorption, 168; omentum, 168; absorption and heat and cold, 168; peritonitis, 169, 238; eventrution, 170; blood vessels, 170; lymphatics, 170; vegetative nervous system, 171; sensitivity, 172; pain, 173; ulcerative processes, pain, 174; diaphragm, 176; omentum, 176; intraabdominal pressure, 181; diaphragm. hernia, 182; tumors, 183; enteroptosis, 183; hernias, 165; peritonitis, 186; literature, 186-189; peritonitis, 238; parietal perit. and reflex action, 239; resistance of, 241, 247; difference of absorption power between parietal and visceral p., 245; bactericidal property, 246; peritoneal irritation, 248; polyserositis, 255
- Peritonitis, 238; resistance of bowel, 55; Murphy button, 55; ascites, 122; bile peritonitis, 139; and food, 169; post-operative preventatives for, 170; abdominal adhesions, 210; ileus, 213; paralytic ileus, 221; bowel contents, 221; cecal distention, 222; absorption, 226; fr. trauma to bowels, 233; nerve involvement, 238; bacterial p., 239; gangrenous p., 240; chronic p., 240; streptococcus p., 240; pneumococcus p., 242; suppurative p., 243; course of the disease, 244, 245; danger of saline solution, 245; secondary abscesses, 245; phagocytosis, 245; leukocytosis, 247; death from p., 248; intestinal paralysis, 249; singultus and vomiting, 250; hematemeses, 250; drainage, 251; tamponade, 251; operations, 252; chronic p., 253; adhesions, 254; polyserositis, 255; appendiceal p., 260; pain, 260; renal abscess, 306; tetany, 361

- Phagocytosis, 245  
 Pharynx sphincter of, 25; diverticuli, 26  
 Phlebosclerosis, 237  
 Phlegmon in esophagus, 28; of bone marrow, 460, 481  
 Phosphorus poisoning, 113  
 Phthisis, phthisical habit, 184; urine, 308  
 Pineal gland sexual precocity, 326  
 Pituitrin, 328  
 Placental circulation, 376  
 Pleura, 162; abdomen in bacterial infection, 242; capillary adhesions, 374; pleura, reflex, 380; Paccini bodies, 380; pain, 380; pulmonary tonus, 386  
 Pleural cavity serosa, 162, 374; obliteration in pneumothorax, 384  
 Pleural reflex, pneumothorax causing death, 381  
 Pleuritis, 383; exudative, 385; death due to kinking of vessels, 385; atelectasis, 385  
 Plexus of Auerbach, 22, 43, 53, 198; Meissner's, 43, 198; choroid plexus, 404  
 Plexus solar, inhibitory center, 44; injury, gastr. ulcer, 76; chr. pancreatitis, 101; peritoneum, 171  
 Pneumatocele, 11  
 Pneumonia, abdominal rigidity, 239; pericolicitis, 254; post-operative, 373, 395; colds, 319; trauma, 398  
 Pneumothorax mediastinum, 358, 362, 379, 382  
 Poisoning effecting liver, 113; phosphorus, chloroform, 113; enteritis, 204; by lead, 221; kidney fr., sublimate, uranium, 292; from alcohol increase of spinal fluid, 408; epilepsy, 418  
 Poliomyelitis, 459  
 Pollacisuria, 284, 319  
 Polyserositis, 255  
 Polyuria, 281; prostatic hypertrophy, 285; pollacisuria, 319; hypophyseal extract., 328; Basedow, 351  
 Portal vein Eck's fistula, 110; anastomosis with renal art., 117; ligat., 117; thrombosis, 118; occlusion, 118; infection of liver, 135  
 Portal system, spleen, 155  
 Position sense of muscle, 432  
 Precipitins antibodies, 246  
 Precocity, sexual, 326  
 Pregnancy, salivation, 5; cholesterin, 132; extrauterine pr., 166; intraabdominal pressure, 183; renal ptosis, 299; enlarged renal pelvis, 303; cystitis, 318; tetany, 360; dyspnea, 386  
 Pressure in esophagus, 28; in bile ducts, 129; intraabdominal, 181; in rectum, 182; garrulitis vulvæ, 182; diaphragm hernia, 182; peristalsis, 182; and tumors, 183; enteroptosis, 183; intraabdominal in ileus, 223, 268; upward pressure, 252; hydraulic in kidney trauma, 295; in urination, 317; tension difference in chest cavity, 374; in lungs, 378; pneumothorax, 379; intraalveolar, 380; in pleuritis, 385; changes in respiration, 387; pressure test of Valsalva, 387; in pleural cavity, 390; low venous pressure and air embolism, 394; in brain conditions, 403; in subarachnoid space, 405; brain pressure and choked disk, 410; dilatation pupils, 410; hydrodynamic in bullet wounds of head, 412; in spinal column, 421; spastic paralysis, 422  
 Prolapsus of rectum, 267; brain prolapse, 415  
 Prostate inflamm., 257; hypertrophy and polyuria, 285; hydronephrosis, 302; tuberc., 311, 322; hypertrophy, function, 323  
 Prostatectomy, 324  
 Proteins metabolism, 111; nucleoproteins, 112; carbohydrates, 114  
 Pseudoarthrosis healing of, 435  
 Pseudotuberculosis, 263  
 Psychical disturbances thyroid, 349  
 Ptosis, 37, 53; of kidney, 299  
 Ptyalin, 4, 5, 42  
 Pulmonary circulation, 377  
 Pulse-rate in brain affection, 403; pulse in cerebrospinal fluid, 404  
 Puncture salt p., 282; lumbar, uremia, 288; in pleuritis, 385; for spinal fluid, 404  
 Pupils dilatation in asphyxia, 389; in brain lesions, 410  
 Purin metabolism of liver, 112  
 Pyelitis, 203

- Pyelography, 303  
 Pyemia, thrombophlebitis, 237  
 Pylorospasm, 50, 78  
 Pylorus, 37-39; movements, 40; acid control, 40; duodenal cap., 40; stenosis, 42; resection, 64  
 Pyonephrosis, 302  
  
 Rachitis, 352; (Rosary) relaxation of muscle, 428  
 Rectal feeding, 81  
 Rectal neuralgia, 207  
 Rectal prolapse, 267; defecation, 269  
 Rectum pressure, 182; margin. current., 195; defecation, 200; tenesmus, 206; proctogenic constipation, 206; carcinoma and constipation, 207; rectoscopy, 223; rupture of, 232; in drainage of Douglas's cul de sac, 253; prostate, 267  
 Reeducation of muscles, 434  
 Reflexes, myenteric, 44; pleural reflex, 381  
 Reichmann's disease, 54  
 Renal artery and portal vein, anast., 117; renal disease, 279; r. colic, 283, 300; insufficiency, 291; renal incarceration, 300  
 Rennin, 42, 57  
 Residual air, 375  
 Residual urine, 318  
 Respiration, gall bladder tracings, 137; chest cavity, 372; thoracic, 373; respiratory center, 375; stimulant CO<sub>2</sub> in venous blood, 375; increase, 376; blood distribution, 377; pressure change, 387; passages and their chronic narrowing, 389; artificial in asphyxia, 390; brain lesions, 409  
 Respiratory center, 375  
 Respiratory failure from bacterial toxins, 248; in asphyxia, 389; artificial respiration, 390; respiratory paralysis and brain affections, 403  
 Retention, 285  
 Retrograde embolism, 391  
 Rheumatism joint disease, 442; rheumatic diathesis, 454  
 Ribs after pneumothorax, 385; rib cartilages, yellow degeneration in emphysema, 387; in kyphosis, 388; in senile spondylarthritis, 388; in tuberc. spondylitis, 388  
 Rupture of bowel, 231; of bladder, 319  
  
 Saline solution as irritant in peritoneum, 243; renal activity, 292  
 Saliva, 1; in fever, 3; composition, 3; function, 3; and digestion, 4; inhibition, 5; stimulation, 6; changes, 6; asialia idiopathic, 6; absence of, 6; anesthesia, 11.  
 Salivary glands, 1; innervation, 1; stimulation, 2; genital glands, 7; ducts, 10; stomatitis, trauma, 10; parotitis, 8; pneumatocoele, 11; saliv. calculi, 11; and foreign bodies, 12; salivary colic, 13; tumor salivarium, 13; degeneration, 13; ligation of ducts, 13; saliv. fistula, 13; literature of saliv. gl., esoph., 30, 35  
 Salivation, 2, 5; in stomatitis, 2; from poisons, 5; in disease, 5; pregnancy, 5; paralytic secretion, 5  
 Salpingitis leucocytosis, 260  
 Scar tissue sarcoma, 154  
 Scrotal hernia, 329; scrotal swelling in elephantiasis, 481  
 Secretin, 57, 95, 125; and bile, 136  
 Secretion paralytic, 5; stomach, 41; pancreatic regurgitation into stomach, 58; of pancreas, 95, 191; of endothelium, 121; format. bile, 123; pancreat. secr. cholecystectomy, 136; of intest. juices, 191; paralytic secretion, 191; of large intestines, 191; absence of pancreatic and diarrhea, 205  
 Sensitivity of abdomin. organs, 172  
 Sepsis peritonitis, 243  
 Septicemia toxic nephritis, 304  
 Sequestrum formation bone necrosis, 463  
 Serosa infection, 243  
 Sexual characteristics secondary, 328  
 Shock from manipulat. of intestines, 228; from anaphylaxis, 229, 289; from exhaustion, 229; CO<sub>2</sub> impoverishment, 229; adrenals, 230  
 Sialolithiasis, 11; sigmoid flexure, 193; defecation, 200; kinking, 207; rupture, 231  
 Sialogogues, 5

- Singultus and peritonitis, 249; diaphragm, 250
- Skeleton readjustment, muscle anlagen, 429
- Skin bronzing after thyroidectomy, 363
- Skull contents, 407; pressure, 407; fracture, 407; and foreign bodies, 411; depressed, 409; elasticity, 411
- Spasmophilia, 360-362; epilepsy, 362
- Spasms, pylorospasm, 50, 78; of anal sphincter, 207; diaphragm, 215; intestinal lead colic, 221; ascariis, 221; ulcers, 222; of tetany, 359; tetacin from ventricular hemorrhage, 417
- Spastic paralysis, 422
- Speech, 7, 13
- Spermatogenesis, 329
- Sphincter of cardia, 22; pharynx, 25; sphincter antri, 38; of Oddi, 102, 105, 134; of intestines, 198; defecation, 200; of anus, 201; of bladder innervation, 315; urinary function, 321
- Spina bifida trophic changes, 459
- Spinal column and intestinal trauma, 230; injury with abdominal rigidity, 239; cerebrospinal fluid, 404
- Spinal cord, conus terminalis and anal innervation, 201; and defecation, 208; sensory roots, 238; resection and abdominal reflexes, 239; bladder innervation, 315; surgical diseases, 421; tuberculosis, gun shot wounds, 421; resection, 422; spastic paralysis, 422
- Spinal fluid, origin, albumen leucocytosis in syphilis, 404; quantity, 405; hydrocephalus, 405; compared to ascites, 408; brain tumors and trauma, 408
- Splanchnoptosis, 184
- Spleen, 70, 111, 121, 129; splenectomy, 148; blood picture, 148; increased resistance of r.b.c. after splenectomy, 149; embryonic spleen, 150; erythropoietic, 150; Malpighian follicles, 150; myelocytes, 150; destruction of blood corpuscles, 150, 155; macrophages, 150; splenic tumor, 150; hemolymph nodes, 151; splenoids, 151; accessory spleens, 151; regeneration, 152; iron metabol., 153, 157; infections, 153, 158; metastasis, 154; digestion, 154; rhythmic changes, 155; splitting of its capsule, 155; psychoses, 155; severe anemia, 155; Banti's disease, 156; splenomegaly, Basedow, 156; jaundice, 156; liver, 156; injuries, 158; literature, 158-160
- Splenectomy, 148; blood increased resistance r.b.c., 149; leucocytic changes, 149; bone marrow, 149, 152, 157; lymph glands, 149; eosinophilia, 149; iron metabolism, 149, 152, 153; thymus hyperplasia, 152; infectious diseases, 153; digestion, 154; constipation, 155; psychoses, 155; anemias, 156; Banti's disease, 156
- Splenic tumor, 150
- Splenomegaly, 156; Basedow, 156
- Spondylarthritis, senile, respiration, 388
- Sprain-fracture, 466
- Status, thymolymphaticus, 355
- Steapsin, 102
- Sterility and thyroid gland, 340
- Stock's collar, 358
- Stomach ptyalin, 5, 36; movements, 36; motor function, 36, 81; divisions, 37; peristalsis, 37, 65; sphincter antri, 38; fasting, 38; defense reflex, 38; food, 38; juice, 38; erosions, 38, 73; antrum, 38; systole, diastole, 39; stimuli, 39; secretion, 39; pylorus, 39; chyme, 40, 56; secretory function, 41; gastric hormone, 41; ganglia, 41; gastr. juice, 41, 47; enzymes, 42; absorption, 42; water, 42; nervous mechanism, 42; pathological changes in gastric motility, 45; vomiting, 45; sensory tract, 46; contractions, 47; hunger, 48, 66; gastric crises, 49; pylorospasm, 50; defective evacuation of food, 51; acute dilatation, 51; arteriomesenteric ileus, 51; gastropptosis, 53; chronic motor insufficiency, 53; asthenia, 53; Reichmann's disease, 54; operation sutures, 54, 63, 66; gastroenterostomy, 54, 57; narrow pass, 56; back flow of intestinal juices, 57, 80; regurgitation, 59; vicious circle, 59; lavage, 60; marginal



- ulcers, 61; hyper-, hypoacidity, 62; pyloric resection, 64; transverse section, 65; total resection, 66 gastrointestinal ulcers, 68; protection against auto-digestion, 62, 69; antipepsin, 70; trypsin causing gastr. ulcers, 51, 71, 76; ligation of blood vessels, 71; capillary thrombosis, 72; hematemesis, 72; bacterial embolism, 74; displacement, 74; constitutional weakness, 78; gastrostomy, 80; secretion, 57, 95; literature, 81-94; cholecystectomy, 137; cholecystenterostomy, 137; slowing of gastric motility, 138; perforation stomach, 166, 172; pain in gastr. ulcer, 174; intra-abdom. pressure, 182; marginal current, 194; achylia and diarrhea, 203; poisoning, 204; tetania gastrica, 361
- Stomatitis and salivation, 2, 10
- Stools, retention, 217; acholic, 124, 128; bloody, 177
- Strangulation ileus, 212
- Streptococcus peritonitis, 240
- Stroma, 27, 448
- Subarachnoid space, 404
- Succus entericus, 97
- Sugars, monosaccharides and intestinal absorption, 193; galactose, 111
- Swallowing, 15
- Synovial fluid, nature, 468
- Synovium in artificial mobilized joints, 468
- Synovitis and synovial cells, 442; absorption, 465
- Syphilis, duodenal ulcers, 75; enteritis, 205; spinal fluid in late, 404; epilepsy, 418
- Syringomyelia, 459; edema, 481
- Tabes, 49; meteorism, 216; tabetic crises, 222, 459
- Tachycardia in exophthalmus, 349, 358
- Talma's operation, 65
- Tamponade of abdomen differentiated from drainage, 251
- Taste, 13; suspension, 14
- Teeth, growth in extirpation of parathyroid, 360
- Tendons, 427; bone fracture, 428; of Achilles and development of calf muscle, 429
- Tenesmus, 206
- Testicle parotitis, 9; tuberc., 311; castration, 324; internal secretion, 328; injury, 329; transplantation, 329; undescended, 329
- Tetany, 359; latent, 360; in pregnancy, 360; spasmophilia, 360; in infections, 361; occupation, 361; ergot, 361
- Thirst, saliva, 3; after bowel resection, 265
- Thoracic duct, 98; colloids, 167; enlargement, emphysema, 386
- Thoracoplasty mediastinum, 358; extrapleural, 383; connective tissue growth, 384
- Thorax, chest cavity, 373; emphysema, 387
- Threshold values, 279
- Thrombokinese, 131
- Thrombophlebitis, 237
- Thrombosis, capillary in gastric ulcer, 72; venous in acute pancreatitis, 104; portal vein, 118; after splenectomy, 148; intestinal distention, 223; after mesenteric injury, 233; embolism differentiated, 237; after appendicitis, 238; varicose veins, 472; infection, 475
- Thymus, 351; hyperplasia, splenectomy, 152; complete thyroidectomy, 341; in Basedow's disease, 351; gland, morphology, 351; metabolism, 351; removal and adipose stage, 352; rickets, 352; calcium balance, 352; function, 352; its ferments, 353; thyroidectomy, 353; death, 354; status thymolymphaticus, 355; chromaffine system, 356; seconds heart death, 356
- Thyroid gland splenectomy, 152; function, 338; thyroidectomy consequences, 339; regulating blood supply to brain, 340; sex, 340; nerve influence to thyroid, 340; metabolism, 340; cachexia thyreopriva, 340; sex organs, 340; ossification, 340; results of complete thyroidectomy, 341; implantation, 342; cretinism, 342; hyperthyroidism, 346; Basedow's disease, 347; exophthalmus, 347; dysthyroidism, 348; nervous system, 349; acute Basedow, 350; thymus,

- 351; parathyroid, 359; complete removal and bronzing of skin, 363; literature, 366-371
- Tongue, 13; function, 13; nerves of taste, 13; taste, 14; speech, 14; removal, 14; deglutition muscles, 15; paralysis, 17
- Tonsils duodenal ulcers, 75
- Tonus of muscles, 428
- Torsion of viscera, 215; of kidney, 300
- Torticollis, 452
- Toxemia due to peritonitis from toxin forming and putrefactive bacteria, 240; urinary, 287
- Toxins, bacterial and paralysis of vasomotor center, 248; intestinal, 225
- Trachea, 30
- Tracheal stenosis and thymus, 355
- Traction diverticuli, 25
- Transfusion of blood, 474
- Transudate ascites, 121
- Tremor in Basedow's disease, 350
- Trendelenburg posit., circulatory changes, 390; operat. for pulmonary emboli, 390
- Trypanosome causing goiter in Brazil, 346
- Trypsin, 57; gastric ulcers, 59, 71, 96, 104; enterokinase, 190; treatment of tuberculous fistula, 466
- Trypsinogen, 97
- Tuberculosis of lymph nodes of neck and dry mouth, 7; of epiglottis, 20; duod. ulcers, 75; acholic stools, 124; spleen, 156; enteroptosis, 184; enteritis, 205; intestinal stricture, 236; renal, 294, 307; congenital, 310; erotism, 311; of parathyroid, 361; closed pneumothorax, 383; encapsulating pulmonary, 384; spondylar, 388; of vertebræ, 421; of bone, 466; fistula, 466
- Tumors, submaxillary, 6; parotid, 6; tumor salivarium, 13; splenic and cirrhosis liver, 121; splenic, 150; intraabdominal pressure, 183; intraabdominal-twisting, 215; prostatic, 323; of hypophysis, 327; of mediastinum, 357; brain tumors, 403; brain tumors, increase of cerebrospinal fluid, 408; of cerebello-pontine, angle, 420
- Typhoid peritonitis, 240; muscle regeneration, 435
- Ulcers of esophagus, 28; gastric pain, 47; marginal, 61; jejunal, 62; gastro-intestinal, 68, 74; leg ulcers, 71; duodenal, 74; intestinal, 205, 236; intestinal spasms, 222; stercoreal, 223; appendiceal, 259; peptic, 260
- Uranium poisoning, 292
- Urea, 279, 287; decomp. into ammonia in cystitis, 319
- Uremia, 286; lumbar puncture, 288; surgical, 288; venesection, 294; after vesical rupture, 321
- Ureters, 284; back flow in hydronephrosis, 301; peristalsis, 302; tuberculosis, 308
- Urethra, 319, 321; prostatic, 322
- Urine and peritoneum, 167; urine, 284; innervation, 285; concentration, 286; albuminuria, see there, stagnation, 304, 319; difficulty in voiding, in prostatitis and pregnancy, 304, 323; in phthisis, 308; composition, 313; in gout, 313; bilharzia, 313; fibrinuria, 314; impulse to void, 316; retention in children, 317; bacteriuria, 318; alkaline, 318; residual, 318; pollakisuria, 319; absorption in bladder injury, 320
- Vaginal drainage of Douglas's cul de sac, 253
- Vagotomy, 50; gastr. ulcer, 78
- Vagus, 20, 40, 50; intussusception, 221
- Valsalva's dysphagia, 18; pressure test, 387
- Varices esophageal, cirrhosis liver, 122; of syphilis, 472
- Varicose veins, 472; leg ulcers, 475
- Vas deferens, peristalsis, 311; prostate, 323
- Veins, 469; portal vein lig. and Eck fistula, 110; saphenous and femoral for permanent drainage for ascites, of mediastinal space, 357, 382; impeded outflow, 382; of the leg and pulmonary emboli, 391; of neck congestion, 406; pressure in, 469; arterial pulse, 471; thrombosis, 472
- Venesection and uremia, 294

- Venous stasis, 408, 451; venous circulation, 460; murmur, 479
- Ventricles cerebral, 405; puncture and epilepsy, 420
- Vertebrae tuberculosis, 421; caries and laminectomy, 421
- Vertebral fracture, 404
- Vesicles seminal tuberc., 311; optic vesicle, ectoderm cells, 457
- Vomiting, 44, 45; innervation, 46; after gastric resection, 67; vomito negri, 73; after splenectomy, 148; fecal and ileus, 212; peritonitis, 249
- War gases, 396
- War wounds, peritonitis, 241; of head, choked disk, 410; to spinal cord, 422
- Wounds in stomach, intestines, 63, 233; in abdomen and omentum, 179, 233; in kidney, 295; of heart, 364; of spinal cord, 421; near spinal cord, pain, 458
- Yellow fever, black vomit, 73
- Zuckergüss leber, 255
- Zymogen, 42, 96









148

APR 13 1928

W0 142 R839p 1923

46310890R



NLM 05236749 1

NATIONAL LIBRARY OF MEDICINE